THE

# REPORT

OF THE

# DEPARTMENT OF PATHOLOGY

OF

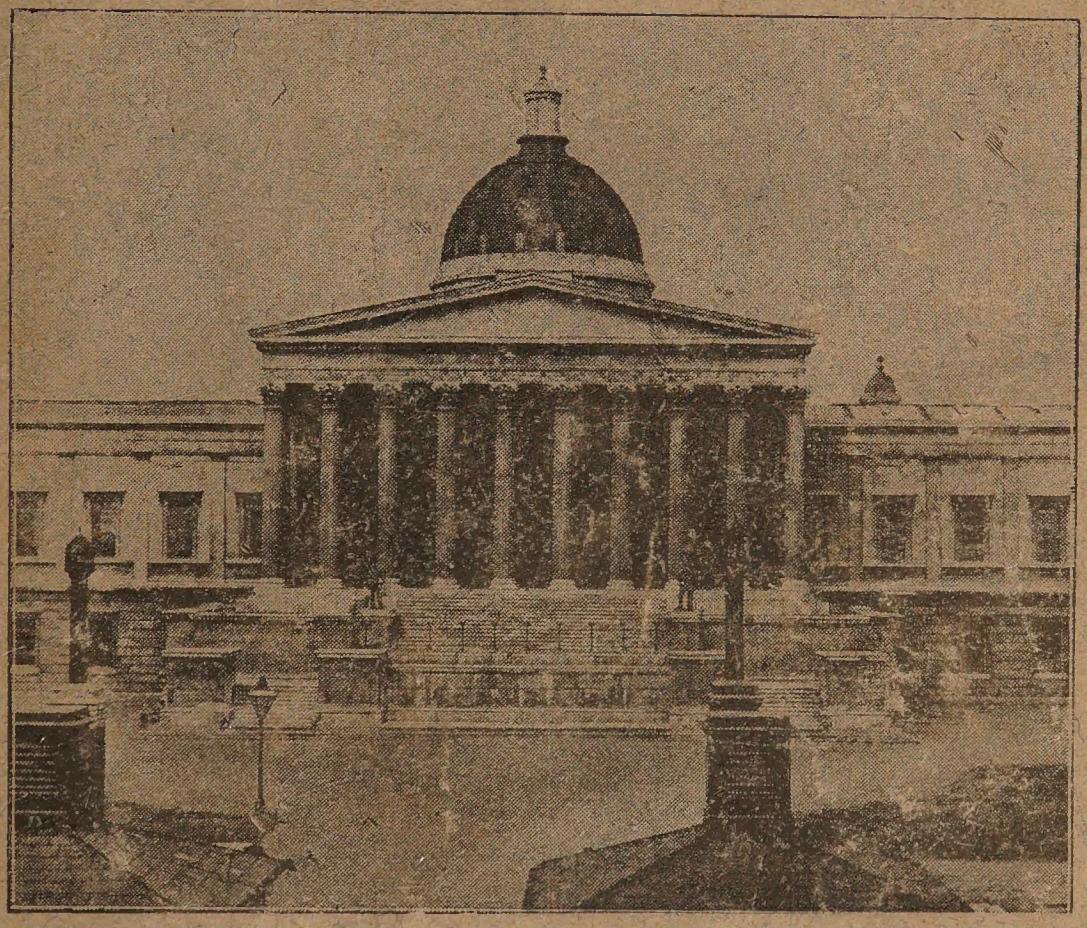
UNIVERSITY COLLEGE, LONDON.

June, 1894.

TOGETHER WITH A

COLLECTION OF PAPERS AND ABSTRACTS PUBLISHED FROM THE LABORATORY.

VOL. III.

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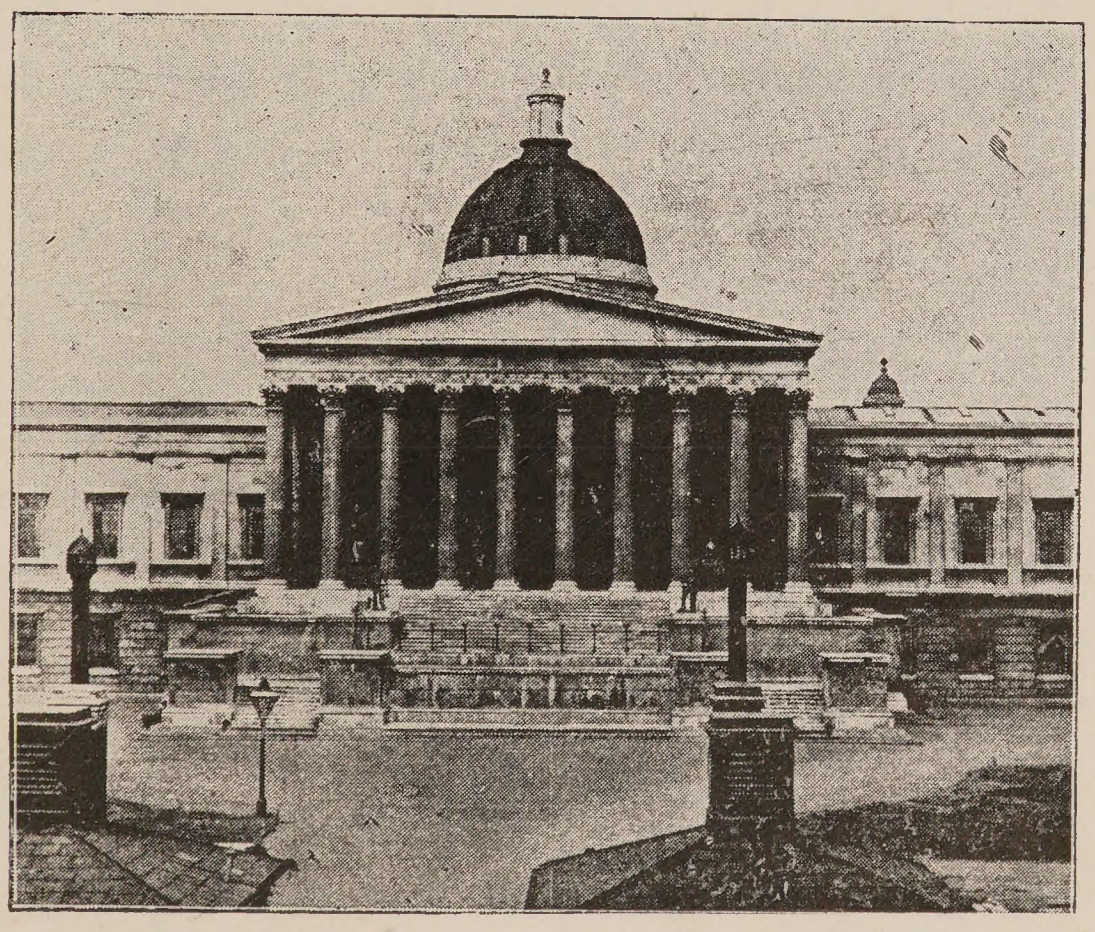


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# INTRODUCTION.

The present volume forms the first which has appeared from the Laboratory this year, and the third since the date of issue last year.

Although this volume contains a very considerable number of Papers, yet, owing to the fact that a large proportion of them are abstracts, the size of the Report is small. To supplement this deficiency, the full Papers which appear in the Transactions of the Royal Society will be shortly bound together and issued as a separate volume of the series.

# INDEX.

## NEUROLOGY.

**W. LLOYD ANDRIEZEN, M.D.**—"The Morphology, Origin and Evolution of the Function of the Pituitary Body and its Relation to the Central Nervous System." Brit. Med. Journal, Jan. 13, 1894.

**RUBERT BOYCE, M.B.**—"A Contribution to the Study of the Descending Degenerations in the Brain and Spinal Cord, and of the Seat of Origin and Paths of Conduction of the Fits in Absinthe Epilepsy." Abstract in the Proc. Roy. Soc., 1894, Vol. 55.

"Note on the Degeneration of the Fifth Nerve." Journal of Physiology, 1894, Vol. 16.

**S. P. KRAMER, M.D., and VICTOR HORSLEY, F.R.S.**—"On the Effects Produced on the Circulation and Respiration by Gunshot Injuries of the Cerebral Hemispheres." Abstract in Proc. Roy. Soc., 1894, Vol. 55.

**A. G. LEVY, M.B.**—"A Research into the Elasticity of the Living Brain, and the Conditions Governing the Recovery of the Brain after Compression for Short Periods." Abstract in Proc. Roy. Soc., 1894, Vol. 55.

**E. L. MELLUS, M.D.**—"Preliminary Note on Bilateral Degeneration in the Spinal Cord of Monkeys (Macacus Sinicus) following Unilateral Lesion of the Cortex Cerebri." Abstract in Proc. Roy. Soc., 1894, Vol. 55.

**J. S. RISIEN RUSSELL, M.D., M.R.C.P.**—"Experimental Researches into the Functions of the Cerebellum." Abstract in Proc. Roy. Soc., 1894, Vol. 55.

**W. G. SPENCER, M.S., M.B.**—"The Effect Produced upon Respiration by Faradic Excitation of the Cerebrum in the Monkey, Dog, Cat and Rabbit." Abstract in Proc. Roy. Soc., 1893.

## CHEMICAL PATHOLOGY AND METABOLISM.

**VAUGHAN HARLEY, M.D., M.R.C.P.**—"Some Effects and Chemical Changes of Sugar Injected into a Vein." Pro. Roy. Soc., 1893, Vol. 54.

"Value of Sugar and the Effect of Smoking on Muscular Work." Journal of Physiology, 1894, Vol. 16.

## BACTERIOLOGY.

**RUBERT BOYCE, M.B., and A. E. EVANS, M.B.**—"The Action of Gravity upon Bacterium Zopfii." Proc. Roy. Soc., 1893, Vol. 54.

"Eine neue Streptothrixart, gefunden bei der weissen Varietät des Madurafusses." Hygienischen Rundschau, 1894, No. 12.

## PATHOLOGICAL HISTOLOGY.

**RUBERT BOYCE, M.B., and ARTHUR GILES, M.D.**—"On Cell Enclosures in Cancer." Trans. Path. Soc., 1893.

# REPORT.

The number of advanced and research Students availing themselves of the greater facilities for work placed at their disposal continues to increase. This is more especially marked in the Chemical Laboratory, which is the latest addition to the Pathological Department. Unfortunately, however, the accommodation is below the requirements of the research and other Students making use of it, and it is hoped that the College authorities will see their way to grant further and more convenient rooms.

The number of senior Students attending the courses of Bacteriology increases. This is in a great measure due to the increased prominence given to this subject in the examination for the Diploma of Public Health. It is now compulsory in most instances for D. P. H. Students to take out a three months' course of Bacteriological Laboratory work. In addition to this, however, advanced Students are commencing to realise the importance of a Bacteriological training to aid them in Diagnosis, *e.g.*, in venereal affections, suspected cases of diphtheria, ophthalmic and skin cases.

Under the new curriculum, Morbid Histology is made compulsory, and for this reason also the number of Students in this subject is increasing. Every facility is given the Student to acquire a practical knowledge of the subject by allowing him the use of the Laboratory and of material in addition to the usual course of practical instruction

in Morbid Histology. It is to be regretted, however, that the Students are apparently prevented, by having to attend so many classes, from availing themselves of the opportunities in this respect, and that the majority consequently confine themselves to acquiring the small amount of Anatomy necessary for the present examination standards.

There is a marked increase in the number of Students attending the lectures on general Pathology.

## RESEARCH WORK.

### I.—General Pathology.

Since leaving the Laboratory, Dr. Otto Lanz has completed his work upon the function of the thyroid gland, and has published a paper on the subject (Zur Schildrüsenfrage, Leipzig, 1894). The experiments made by him in this Laboratory were undertaken to discover, if possible, the seat of origin of the *tetany* observed in cachexia thyreo-priva, both in man and animals. For this purpose, a series of experiments were made in the Dog, in which either the sciatic nerve or the spinal cord was divided, or the motor area on one side removed. He concludes that the spinal cord is the chief seat of the tetany, but that the higher centres also influenced the spasms. In addition to the experimental and clinical observations made by the author, the paper deals succinctly with the most recent knowledge of the development, histology, morbid anatomy, and function of the thyroid, together with the therapeutics of cachexia thyreo-priva.

While referring to this question of the thyroid body, we may note that some experiments recently made in the Laboratory by Dr. Harris and Professor Horsley upon the reduction and oxidation of methylene blue in the tissues (Ehrlich's method) have revealed the interesting fact that Gley's parathyroid body behaves differently to the main mass of the thyroid.

The subject of experimental degeneration in the central nervous system, and its investigation by the Marchi method, is occupying the attention of several investigators.

Dr. Mellus is carrying on the investigations of the descending degeneration following the removal of the various motor centres in the cortex of the Monkey. They show that no special portion of the pyramid is apportioned to any one centre, but that removal of the great toe or thumb area produces a scattered degeneration throughout the pyramid. In the internal capsule, however, a considerable amount of grouping is observable. As will be seen in the abstract, there is found to exist a very considerable amount of *bifurcation* at the decussation, most marked in extirpation of the great toe area, rather than in that of the thumb focus.

An investigation of the mode of termination of the ascending cerebellar tracts has been undertaken by Dr. Patrick to supplement a case of ascending degeneration recently published by him in "The Archiv für Psychiatrie." The results so far appear to confirm the looping described in the case of the ventral cerebellar tract.

Mr. Boyce is continuing his observations upon the removal of the whole or a large portion of one hemisphere. The experiments have been made in a large number of animals, including the Cat, Rabbit, Guinea Pig, Hen, Tortoise, Snake. The results in the Cat have been chiefly investigated, and they show that, as in the Monkey, there is a slight pyramidal bifurcation at the decussation; that previous to the decussation degenerate fibres leave the pyramid at various levels in the mesenaphalon, pons and medulla, and pass backwards, the majority crossing the raphé; that when the quadrigeminal region of the mesencephalon is injured, there is degeneration of the "fountain" decussations of *Meynert* and *Forel*, and that the fibres forming these decussations are continued into the antero-lateral and lateral columns of the cord. Degeneration is also observed in the posterior longitudinal bundle on the same side as the injury to the mesencephalon; these fibres are continued into the anterior column of the cord. *Meynert's* and *Forel's* commissures in front of the third ventricle have been also found degenerate in cases of hemisection in the mesenaphalon.

The statement of Pitres that the Hen possesses no pyramid has been confirmed by the Marchi method; in the Guinea Pig, likewise, the same method shows that the pyramid crosses into the posterior column. The size of the pyramidal fibres both in the Rabbit and Guinea Pig is found to be very much smaller than in the Cat or Monkey.

An abstract of some of the results obtained above has appeared in "Proc. Roy. Soc.," and will be found in this volume, likewise one on the degeneration of the root of the fifth nerve, published in "The Journal of Physiology"; further papers dealing with similar subjects are in progress.

Dr. Risien Russell has completed his investigation into the functions of the cerebellum, and an abstract of his paper is contained in this volume. The full paper will be published in "The Philosophical Transactions of the Royal Society."

This investigator has also been engaged in tracing the degenerations consequent on ablation of the middle and lateral lobes of the cerebellum by means of the Marchi method. His results, in this connection, form the subject of a paper which has been submitted to the Royal Society. He does not confirm Marchi's statement that there is a direct efferent tract from the cerebellum which degenerates throughout the whole length of the spinal cord after cerebellar lesions. Nor does he agree with this observer that the fillet, posterior longitudinal bundles, cranial and spinal nerve roots degenerate after such lesions. Contrary to the observations of Ferrier and Turner, he finds degeneration in all the cerebellar peduncles after extirpation of the middle lobe.

Another research in which he has been engaged is one dealing with eye movements, the results of which investigation will appear in a paper in the next number of "The Journal of Physiology." The existence of cortical centres for ocular movements, other than that for conjugate turning of both globes to the opposite side, have been demonstrated. The influence of the cerebrum and cerebellum on eye movements has been dealt with, as also the action of anæsthetic agents in reproducing ocular deviations, experimentally produced and recovered from. And ocular deviations consequent on lesions of the labyrinth and auditory nerve have also engaged his attention.

An interesting case of defective development of the central nervous system in a Cat has been carefully worked out by him, and many points of great importance have been the outcome of the investigation. The more important points formed the subject of a communication to the Neurological Society, and the case will probably be published in an early number of "Brain."

Dr. Kramer and Professor Horsley have carried out an extensive series of experiments on the causation—primary and secondary—of death after bullet wounds of the cerebral hemisphere. The primary cause they have found to be arrest of the function of the respiratory centre, thus confirming the view previously enunciated by Spencer and Horsley regarding the sensitiveness of the respiratory centre to shock and rise of the intracranial tension. The secondary cause of death they find to be intracranial hæmorrhage. The full paper will be published by the Royal Society.

Mr. Spencer has during the year been engaged upon the effect upon the respiration and circulation of exciting the cerebrum, and some of the results obtained will appear in "The Philosophical Transactions."

He has also examined the intracranial roots of the vagi and the floor of the fourth ventricle from the same point of view. The work is intended not only to throw further light upon the Physiology of the central innervation of the respiration and circulation, but also to enlarge our knowledge concerning Pathological states known as "Exhaustion," "Collapse" and "Shock," etc.

## II.—Chemical Pathology.

In the Department of Chemical Pathology under the guidance of Dr. Vaughan Harley :—

Dr. Nusserwanji Surveyor carried out a research on the value of $\beta$. Napthol as an intestinal disinfectant, the results of which will shortly be published.

Dr. White, in a research into the effect of repeated hæmorrhage on the chemical changes in the composition of the blood, has found that the specific gravity did not fall in the same ratio as the hæmoglobin, but that whilst the total proteids fell with each successive bleeding, the fibrin on the other hand increased. The salts were very little affected, whilst the cholesterin lecithin and fat of the blood tended to increase in quantity with each hæmorrhage.

Dr. Smith has studied the chemical composition of various ovarian cysts with the view of finding, firstly, whether pseudomucin is of any diagnostic importance, and, secondly, whether the more minute analysis into the chemical composition of such fluids is of any value in diagnosing the position, malignancy, etc., of such cysts.

In conjunction with Dr. Vaughan Harley, Dr. Smith is making a more thorough investigation into the chemical composition of transudations and exudations throughout the body, with special reference to the relation of the specific gravity to quantity of proteids and extractives; also the presence of the various proteids, and the relative quantities of cholesterin fat and lecithin to one another.

Dr. Dudley Cooper, conjointly with Dr. Vaughan Harley, is investigating the metabolism in general paralysis to endeavour to find out the cause of the loss of flesh in such cases.

Mr. Rutter is carrying on a series of experiments into the formation of uric acid in the organism.

Professor Thompson and Dr. Vaughan Harley are at present engaged in a research on the influence of various nerve lesions on the respiratory gaseous exchange.

Dr. Vaughan Harley is continuing his experiments on the destruction of sugar in the animal economy, with special reference to diabetes, and on the assimilation and digestion after pancreatic extirpation.

He is at the same time carrying on a research into the digestive and absorptive powers of the larger intestine.

The chemical composition of the bile in various diseases of the liver is being investigated according as it is possible to obtain material.

## III.—Bacteriology.

In Bacteriology, the investigation of Madura foot, first commenced by Dr. Surveyor and Mr. Boyce, has been actively continued, and has resulted in the isolation, in the case of the white variety of the disease, of a very typical *Streptothrix*. By means of the kind co-operation of Surgeon Lieut.-Colonel Keith and Dr. Boccarro in Hyderabad, Sinde, glycerine agar tubes were inoculated in Hyderabad with the discharge, and from these Mr. Boyce has succeeded in obtaining the *Streptothrix*, which produces local inflammatory lesions in the lower animals, *e.g.*, rabbits.

Dr. Surveyor has recently returned from India, and is engaged with Mr. Boyce upon the further investigation of Madura disease.

Dr. Bruschettini is engaged upon the subject of tuberculosis immunity, and upon the influence of the products of virulent bacteria upon the non-pathogenic, in reference to the question of inducing pathogenicity.

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January 13th, 1894.

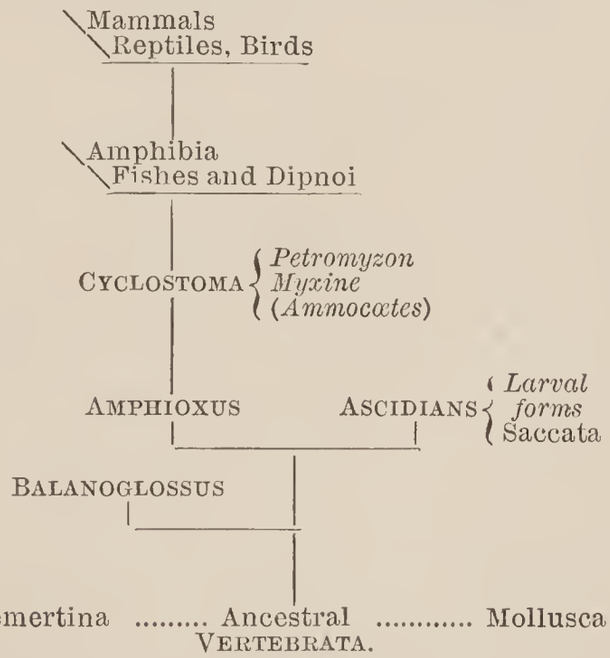
# THE MORPHOLOGY, ORIGIN, AND EVOLUTION OF FUNCTION OF THE PITUITARY BODY, AND ITS RELATION TO THE CENTRAL NERVOUS SYSTEM.[1]

BY W. LLOYD ANDRIEZEN, M.D.LOND.,
[From the Pathological Laboratories of University College, London, and the West Riding Asylum, Wakefield.]

THE pituitary body occupies the position the pineal body once did. The latter was even suppposed to be the seat of the soul (Descartes), the pathway of a gullet (Owen, de Blainville), etc., till De Graaf and Spencer in 1886 showed its true significance.

My researches were commenced March, 1891. The material used was a large number of specimens, living and preserved, of larval and young amphioxus, larval and adult ascidians (oikopleura, salpa, pyrosoma), young and adult balanoglossus, ammocœtes and adult petromyzon, various fishes, and larval and adult amphibians. I have made further studies more recently on fœtal and young kittens, and the pituitary organs of the rabbit, rat, monkey, and man to elucidate points which arose from the work with the lower forms.

*Zoological Tree (Phylogeny) of Vertebrata.*




[1] Abstract of a paper read in the Section of Pathology at the Annual Meeting of the British Medical Association held at Newcastle, August 4th, 1893.

Authors who had hitherto studied the pituitary body began from myxine upwards, for example, Müller, *Virch. Arch.*, 1871, and others in his footsteps. Many clues were thus lost which only the investigation of the earliest, and especially acraniate vertebrates, could afford. Real light is thrown only by the investigation of ammocœtes (larval petromyzon) and lower forms, for these evidence a twofold function of the pituitary, and explain its twofold structure, for even in the highest mammals and man it has a twofold structure, and represents a double organ.

My investigations in larval amphioxus showed that the "subneural gland" and its relations to the neural tube are of importance. This organ exists (*a*) in a position corresponding to the pituitary of higher animals, (*b*) presents the histological structure of a secretory gland, (*c*) is developed from buccal epiblast, and (*d*) has anatomical connections both with the brain floor and the buccal roof. It is obviously the homologue of the pituitary. To particularise: observations showed the development of a small and specialised group of nerve cells in the basal part of the brain cavity (thalamocoel) with which the subneural gland came into relationship. The central canal of the spinal cord, traced forward into this region, was seen to undergo dilatation into a distinct ventricle. (Adult forms do not exhibit this so well.) A duct was further formed, which had a capillary lumen lined by ciliated epithelium, and establishing a connection between the buccal cavity and the "ventricular" cavity (thalamocoel). (It is not to be confounded with Rathke's diverticulum of the hypophysis, which can be seen in all embryonic mammals, including man, and is a blind tube denoting the tract of invagination and sinking of the hypophysis.) The nerve cells (before mentioned) aggregated around the neural opening of this duct into the neural tube; the epithelial cells (subneural gland) aggregated around the lower or buccal opening of the duct.

Owing to the degenerate character of amphioxus and its asymmetrical development in later larval life, certain alterations take place. These are to be looked upon as adaptive, and not genetic or fundamental; the notochord elongates anteriorly, the subneural gland, and oral cavity are displaced laterally; even the myotomes get displaced, this last condition persisting to adult life (*cf.* similar adaptive asymmetrical changes in flat fishes and molluses). The study of other allied forms enables us to "allow" for this disturbing factor.

The study of the larval ammocœtes affords a more distinct realisation of the conditions foreshadowed in larval amphioxus, and one undisturbed by adaptive (or adventitious) asymmetry.

The pituitary in amphioxus and ammocoetes is a threefold structure, namely: (*a*) a subneural glandular organ, primarily median, and originating from the epithelium of the buccal roof at the orifice (*b*) of a duct lined by ciliated epithelium, which affords a communication between the buccal and neural cavities, and (*c*) a group of nerve cells around and at the back of the upper opening, where the duct widens into the ventricular cavity. This widening part is the infundibulum, and the duct may be called the buccal infundibular duct.

It occurred to me that this duct would at once allow a current of water to enter the ventricle from the buccal cavity. To demonstrate it was the crucial point; by using a very fine emulsion of carmine suspended in the water in which these animals lived, and passing it towards them by a fine nozzle, a slow stream could be passed from the bottle containing the carmine emulsion. After an hour and a-half to two hours, on killing the animal with $OsO_4$, and observing it under the microscope, a number of fine carmine particles could be seen in the duct, and lining all over the ventricle. By keeping the animals alive longer exposed to the carmine stream, similar particles could be traced step by step into the central canal of the cord; after a day along the whole length of the cord, and right up to the posterior free end of the canal, where the spinal canal opened into the exterior by the blastopore (neurenteric canal).

It was thus obvious that there was a *raison d'être* for the buccal-ventricular duct where the stream of water entered, for the ciliated epithelium of the central nervous cavities which propelled this stream, and for the neurenteric aperture[2] which formed the outlet for the exit of the water current after its passage through the central nervous system.

It was thus shown that the buccal-ventricular duct served as the inlet whereby a stream of oxygen-bearing water could enter the central nervous system; and as the water (in which the animal lived) streamed slowly through the nervous tube by ciliary action, the nerve tissue would be enabled to take up oxygen from the water current, while the gaseous ($CO_2$) and other products of the activity of the nerve tissue would similarly pass into and exit with the outflowing stream from the posterior (and still patent) end of the neural canal.

The duct portion of the pituitary was then the inlet of a water-vascular stream which brought in oxygen to the central nervous system, while similarly the neurenteric canal, which opened into the exterior posteriorly, served as the outlet to carry away the waste products by means of the outgoing water-vascular current in ancestral vertebrata.

*A similar mechanism of a water-vascular current irrigating the nerve tissues* is also found in a striking form in the nervous system of various larval and adult ascidians, in balanoglossus,[3] ammocoetes, etc., while in the phyla of the animal kingdom which approximate morphologically and genetically to ancestral vertebrata (namely, larval forms of mollusca and of echinoderma) water-vascular systems of a complex kind are found permeating the tissues and organs of the body generally—being a widespread biological phenomenon in ancestral vertebrata and their allies.

A complete zoological survey enables us to formulate facts in the following terms: that a water-vascular system permeating the body tissues, and serving for the in-bringing of oxygen, and the out-taking of waste products, and having

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[2] The researches of Kowalevsky on Ascidians, of Götte on Amphibia, of Kölliker, His, Balfour, all agree in showing the existence of a neuranal canal.

[3] The larva of balanoglossus (tarnaria), and the bipinaria larva of asteroids (echinoderms) also show water-vascular organs, showing the extreme antiquity of this system, and its deep significance in the animal kingdom.

inlets and outlets communicating with the aqueous medium in which the animal lives, preceded, in point of time, the development and elaboration of a true blood-vascular system.

Study of the degenerate ascidian Botryllus affords an instructive lesson. As the result of a fixed parasitic degenerate life, the olfactory organs and centre go, the visual organs and centre cease developing, and also atrophy. In the larva of botryllus the thalamocoel gets thickened in its basal part, where an aggregation of nerve cells can be seen as in other forms mentioned.

A tube is also formed connecting the stomodaeum with the thalamocoel (the buccal with the neural cavities). In the larval active form, the stream of oxygen thereby enters and aërates the brain; in the adult the fixed parasitic life demands neither brain nor body activity in the same degree; and, in correlation with that, and, owing to adaptive modifications of the head region generally, the duct closes and is obliterated.

The buccal-ventricular duct is ventral to the anterior end of the central nervous system. Its pore is a ventral neuropore, which marked the communication between buccal and ventricular cavity, and the inlet of the water-vascular current.

An earlier condition of affairs, somewhat previous in point of time to the ventral neuropore and pituitary formations, was the formation of a dorsal neuropore, which, however, soon closed in amphioxus, though in ascidians and balanoglossus the dorsal neuropore persisted into adult life. In balanoglossus a dorsal neuropore is seen, in which the opening reaches the brain surface only; in the more active young the brain is hollow, and its cavity (ventricular cavity) is in direct communication with the duct, which thus allows a stream of water (driven by ciliary action) to irrigate the brain tissue more intimately. In appendicularia and other larvalia, and in salpa (a free-swimming tunicate) a dorsal neuropore is present. In the young of salpa this ciliated tract or funnel opens into the brain cavity, though in the adult both brain cavity and ciliated tube get obliterated, and the brain becomes solid. The dorsal neuropore is also present in ammocoetes as a very transient phase. In higher forms rudiments of it (not functional) have been observed in elasmobranch fishes by Van Wijhe (1882), and by Kupfer in his monograph on Accipenser sturio (1893). It is also present in embryos of birds (Van Wijhe). It is important to note that the dorsal neuropore or its vestige is anterior to the pineal body, which arises from the posterior edge of the roof of the thalamocoel), and dorsal in position to the olfactory centres (which arise in the anterior edge of the floor of the thalamocoel). The dorsal neuropore is a more archaic structure, and represents the region where the anterior dorsal end of the nerve tube failed to sink into the tissues deeply like the rest of the nervous system. The ventral pituitary duct (buccal-infundibular duct) was a later formation in the race, appears later in the individual, and achieved a higher grade in development, having associated with it the complex structure of the glandular pituitary (anterior lobe) and the nervous pituitary (posterior lobe of higher forms). This view is

strikingly borne out by the recent investigation of Salensky on pyrosoma.[4] This organism presents two morphological types (zooids), namely, the cyathozooid (a sexually produced rudimentary zooid) and the aseidiozooid (a more mature budded-out form). The former presents only the dorsal ciliated pit; the latter, which is more advanced, presents also the dorsal pit (at first), followed by the later and more developed ventral duct (pituitary duct) of stomodoeal origin. The obvious necessity of supplying a considerable amount of oxygen to the central nervous tissues was thus realised, though imperfectly, in balanoglossus, salpa, appendicularia, and the two types of pyrosoma by the dorsal neuropore and its connections with the ventricular cavity dorsally. At a later stage and in the more highly-developed ascidizooid of pyrosoma, in salpa, in amphioxus, and in ammocoetes this was realised by the more complex duct and its associated organ, the pituitary, the further significance of which now remains to be seen.

These organs associated with the duct form, as mentioned before, are, (*a*) a glandular secreting structure of buccal origin (epiblastic), and (*b*) a nervous centre developed at the base of the brain at the orifice where the duct lumen widened into the ventricular cavity. Such a nervous organ situated at the orifice whereby the stream of water enters the cavities of the central nervous system would be sensitive to the quality of the water which passes over it. This is no isolated phenomenon, for we find a striking analogy in the osphradial organ and ganglion of mollusca, which is situated at the entry of the mantle or respiratory chamber and serves to test the quality of the water which passes over the respiratory organ. The obvious significance of the group of nerve cells which form the posterior lobe of the pituitary and are continued a little way up the infundibulum is that—namely, to be sensitive to the noxious quality or otherwise of the water which would enter and permeate the central nervous system. Similar specialised sensitive structures develop according to a well-recognised biological law at other orifices (buccal, respiratory, generative, etc.). From this group of mainly fusiform nerve cells peripheral processes can be traced which run down to and end freely at the buccal orifice of the duct and in its lumen, and in the newborn and fœtal kitten brain by the method of staining with chromate of silver, the central processes of these cells can be traced far backwards towards the pons. In ancestral vertebrate forms, where the pituitary duct was still functional and formed the inlet of the water-vascular stream, the sensitive nerve centre at its orifice would also be functional, while later, with the advent and growth of a blood-vascular system permeating the central nervous organs, and thereby bringing oxygen to the nerve tissues, the necessity for a water-vascular current would no longer exist. The pituitary duct thus closes up and gets obliterated (by a growth of vessels, of connective tissue, and neuroglia), and the sensory nervous structure in connection with it functions no longer and atrophies. All the above agree with facts of observation; the posterior or nervous lobe of the pituitary begins to atrophy in all forms above larval

[4] *Zool. Jahrbücher*, v, 1.

petromyzon, and in the mammals and man is an exceedingly atrophied organ possessed of very little besides neuroglia.

The *ensemble* of evidence recorded tend to prove that the pituitary is not a simple structure having one simple function, but a complex organ composed of at least three parts, namely: (*a*) An anterior secreting glandular organ (of which more anon); (*b*) a water-vascular duct; (*c*) a posterior sensitive nervous lobe, of which the last two, namely, the duct and nervous lobe, were morphologically well developed and functioned in ancestral vertebrata, but have become obliterated and atrophied in structure and function for ever in all forms above larval acraniates and ammocoetes. The posterior lobe begins to lose its nerve substance as we ascend the animal scale from ammocoetes upwards. In the larva of frog or salamander the progress of atrophy can be clearly recognised. Portions of the nervous infundibulum get thinned down here and there, in places being reduced to a mere thin layer of ependyma covered by a highly vascular pia, while the ingrowing loops of blood vessels push the ependyma in here and there towards the infundibular cavity, giving this part of the posterior lobe of the pituitary the appearance of a highly vascular plexiform saccular structure (saccus vasculosus of fishes and amphibia). Traced up to man, the posterior lobe represents little beyond a neuroglia remnant of what was once a functional portion of nerve tissue in ancestral vertebrata.[5]

The glandular secreting portion (anterior lobe) of the pituitary is the type of a secreting structure of epithelial cells arranged in lobules and ascini, with many ducts opening into one main duct (the buccal-ventricular or pituitary duct). Histological examination of it in ammocoetes and young fishes shows it, and also shows its relation to the infundibulum and posterior lobe.

The minute structure and microchemical staining reactions all agree that the glandular epithelioma is secretory[6]; and in these early forms the secretion poured into the duct would be carried with the water-vascular stream through the central nervous system.

Such a phenomenon is significant. It cannot be that a definite glandular secreting organ, developed at the orifice of a definite tube, and having its secretion carried through the said tube and so through the central nervous organs, mixed up with the oxygen-bearing water, and therefore coming into intimate contact with the nerve tissues, is non-significant. It is of some use to the organism, and must especially be so in the economy of the metabolism of the nerve tissues, just as much as the oxygen borne by the water current is. Its action would be one of two things, namely: (*a*) a trophic action on the nerve tissues, enabling them the more readily

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[5] The replacement of a water-vascular by a blood-vascular system in the animal kingdom, the obliteration of the water-vascular orifice and infundibular duct, the atrophy of the sensitive nervous structure connected therewith, the closing, similarly, of the outlet (neurenteric canal) of the water-vascular stream, and the final and gradual degeneration of the cilia in the central epithelium which formed the motive power which propelled the water current through the central nervous system—all seem an instructive lesson in evolution and dissolution.

[6] See evidence collected by Boyce (*Jour. of Pathol.*, 1892-93) and Beadles.

to take up and assimilate the oxygen of the water-vascular current; or (*b*) a destructive action, serving to neutralise and render innocuous the waste products of the activity of the said nerve tissues. Between two such alternatives it is difficult to decide, and after all it may be that at the root the two functions are intimately related; an adequate assimilation of the oxygen by the nerve tissues securing an adequate destruction (by oxidation) of the material products of nervous metabolism.[7]

We have seen how, with the development of the blood-vascular system invading the central nervous organs, and thereby bringing oxygen to the nerve tissues, the need for a water-vascular current no longer exists, and how the pituitary duct gets closed, the posterior neural canal (neurenteric canal) closes, the ciliated epithelium begins to show atrophy of the cilia, and the nervous tissue of the posterior lobe of the pituitary functions no longer, is not needed, and begins to die and dwindle away.

Is the secretion of the anterior glandular lobe needed after the closure of the pituitary duct and the cessation of the water-vascular stream which once carried it to the nerve tissues? Yes, for the oxygen is now brought to the nervous tissue by the blood-vascular stream. Hence the pituitary gland continues to produce its secretion, which, now that its duct is obliterated and the gland changed into a ductless gland, becomes an "internal secretion," which, being absorbed by the lymphatics,[8] and therefore passing once more into the circulation, enters into the nerve tissues with the blood-vascular stream.

The fluid which was once passed as an "external secretion" with the water current which permeated the nervous system is now reabsorbed into the lymphatics, and goes with the general blood current once more to the nerve tissues. It still acts on the nervous system; its old trophic function is not abolished under the new *régime*, but maintained. (In fact the activity of the gland would seem to be for a time at least increased, judging by the large relative size and great vascularity of the organ as we pass up from the cyclostoma to fishes.)

As we ascend the vertebrate scale still higher, through amphibia to mammals and man, its relative size does not keep pace with the increased growth of the nervous system—an indication probably that, having attained the acme of its activity in lower vertebrates, it is in higher forms already beginning to show signs of diminishing activity, though, of course, still functionally active even in man.

In passing, a reference is needed to the views on the oral cavity as representing a pair of coalesced (right and left) gill slits, and that the hypophysis was the representative of a pair of preoral gill arches (Dohrn), which has been carried

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[7] Thus Hoppe-Seyler has shown (Virchow's *Festschrift*, 1891) that in the functional activity of cells the formation of lactic acid—a toxic metabolic by-product—is due to insufficient oxygen supply, and that if abundant O is supplied, the tissue takes it up and further oxidises the lactic acid into $CO_2$ and $H_2O$, which are eliminated. Other and similar examples occur in the animal economy.

[8] As proved by actual histological examination; (*Cf.* thyroid) evidence accumulated by Horsley, Boyce, etc. (*Univ. Coll. Pathol. Lab. Reports*, 1893-4)

to an extreme by Marshall (1882). These views were partly the outcome of an erroneous interpretation of the value of branchiomerism in determining metameric segmentation of the head, and partly the outcome of a similar attempt to apply the "vertebrate theory" of Goethe to the formation of the anterior head region (Goethe's and Oken's views, developed by Owen). Both views have been shown to be unsupported by facts, and a more correct orientation of the head structures (both oral and preoral) have shown (Van Wijke, 1882; Ahlborn, 1884; Gegenbaur, 1887; Lankester, Rabl, Hatschek, 1888-92) that all gill arches and gill clefts are *post*-oral, that analogous structures do not exist in oral or preoral regions, that branchiomerism is not parallel, and does not correspond with metamerism.

A survey and investigation based on all classes of vertebrata show that the hypophysis occupies the position and relationship to the other structures which may be condensed into the following table:

*Relation of Pituitary to other Nerve Centres and Head Structure, in order from before back.*

| | | | |
|---|---|---|---|
| Nerve centre. | Olfactory centre. | Posterior lobe of pituitary | The bulbo-spinal centres. |
| Nerves. | Olfactory nerves. | Hypophyseal nerves. | Bulbo-spinal nerves. |
| Distribution. | Epithelium of nasal sac. | Pituitary duct and gland (anterior lobe). | Buccal, etc., and general cutaneous. |
| Body region. | Pre-oral (prostomial). | Oral. | Post-oral (branchial, etc., and general body). |

The old views of Blainville and Owen that the pituitary represents the pathway of an invertebrate gullet were based on erroneous interpretations of zoological facts; a revival of similar views—for example, in making the third ventricle represent a cephalic stomach as in crustacea, and the central canal of the cord the remnants of a pre-vertebrate gut (Gaskell and Bland Sutton)—has failed through want of adequate zoological, histological, or pathological evidence; while, on the other hand, Hubrecht's and Lankester's view of the origin of vertebrates from platyhelmia, of which living nemertinae are the nearest allies, still remains established, in contrast to the others and further evidence is daily accumulating.

In regard to the size and weight of the pituitary, its prevalent variations—from 0.3 to 0.6 g. (Quain, 1881); and 0.4 to 0.9 g. (Boyce and Beadles, 1892)—would bring it under the Darwinian law of panmixia; if so, the indication being what study of lower vertebrates shows, namely, that it has probably passed the acme of its activity, and in man is functioning less vigorously.

A reference is needed to the thyroid and its functions in lower vertebrata before concluding. The author has investigated this organ during the last year, and at the discussion

three days ago (August 1st, 1893) on the function of the thyroid was able to state that the origin and mode of evolution and its activity in lower forms indicates that the thyroid is to be looked upon as associated anatomically with a primitive respiratory system, and physiologically with the respiratory gaseous exchange of the blood and tissues; while the phenomena following its destruction by disease or experiment are to be interpreted as at the bottom a disturbance of the gaseous metabolism and malassimilation of oxygen by the body tissues, to which are probably correlated the subnormal temperature, weakness, twitchings, excess of fat, and languor and weakness of muscular and brain tissues consequent upon such destruction.

Having regard to the obvious features of parallelism which both organs, according to the author, thus exhibit in their early evolution in vertebrate animals, a physiological relationship would seem to exist between the thyroid and the pituitary glands. If such an explanation is correct, the recent results of enlargement (? compensatory) of the pituitary after thyroidectomy may be explained; for the concordant results of Stieda, Hofmeister, and Gley (1892-3), go to prove such an enlargement of the pituitary after thyroidectomy. But otherwise the parallelism fails, for the pituitary belongs both anatomically and physiologically to the central nervous system, and the thyroid to the respiratory function of the blood-vascular system, and thereby of the tissues generally.

The main conclusions from the above lines of investigation all point to the important trophic influence of the pituitary gland on the central nervous system of vertebrates. If the origin and mode of evolution of its function be such, we ought clearly to get definite and predicable effects from the ablation or destruction of the gland whether experimentally or by disease. The evidence of disease has not yet thrown light on the nature of its function and experimental destruction (so far as the author is aware) has given negative results (Horsley, 1886; Gley, Marinesco, and others, 1892-3; and literature to end of March, 1893). Negative results are, however, of doubtful value, and cannot overweigh the positive evidence derived from comparative study based on sufficiently extensive material, and where all the facts concerning origin and mode of evolution of both structure and function are harmonious and consistent. The author therefore ventures to state what such predicable effects might be in successful cases of ablation of the pituitary. For it was stated above as the result of the present investigation, that the pituitary gland exercises a trophic action on the nerve tissues, which in more definite terms meant "enabling them (*a*) to take up and assimilate oxygen from the blood stream, and (*b*) to destroy and render innocuous the waste products of metabolism, and that at root these two functions are intimately related, and are really at root part of one process (vital or bio-chemical); an adequate assimilation of oxygen by the nerve tissues securing an adequate destruction (by oxidation) of the waste products."[9]

The predicable results of the ablation or destruction of the

[9] *Vide supra* and footnote from Hoppe-Seyler.

gland would therefore be those due to (*a*) a malassimilation of oxygen by the nerve tissues, and simultaneously (*b*) an insufficient destruction, and therefore accumulation of waste products ; thus bringing about a rapid nutritional failure and death of the central nervous system. In general terms we would therefore expect in the animal :

1. Depression and apathy (the commencing failure of activity in the nerve centres) ; and
2. Muscular weakness (the first peripheral effect).
3. Loss of fine co-ordination and equilibration (correlated to 1 and 2), and
4. The development of twitchings and irregular contractions (spasms) of the muscles (in relation to the further progress of nutritive failure of the nerve centres).
5. A want of sufficient heat production, and subnormal temperature.
6. A wasting of the body tissues (in relation to the more rapid failure of nutrition of the central nervous system).
7. A probable compensatory polypnœa, or attacks of dyspnœa (the peripheral indication of the failure of the nerve centres to assimilate oxygen).
8. A rapid progress towards death. Future research must negative or confirm these statements.

In conclusion, the author would wish to call attention to the undoubted value of studying biological problems (to the physiologist and pathologist) from the comparative and zoological standpoints, and by experiments on the lower vertebrates, to obtain light more particularly *on the origin and evolutions of structures and functions* and to understand their *raison d'être* in relation to the higher animals and man, following especially the method of the great Darwin.[10]

[10] A future communication will deal with the subject of pituitary feeding and injection in some forms of nervous and mental disease.

[*From the* PROCEEDINGS OF THE ROYAL SOCIETY, Vol. 55.]

# "A Contribution to the Study of Descending Degenerations in the Brain and Spinal Cord, and of the Seat of Origin and Paths of Conduction of the Fits in Absinthe Epilepsy."

By RUBERT BOYCE, M.B., Assistant Professor of Pathology, University College, London. Communicated by Professor V. HORSLEY, F.R.S. Received February 8, 1894.

(From the Pathological Laboratory of University College, London.)

(Abstract.)

For the purposes of this research, the following are the experiments which have been performed in the cat :—

I. *Lesions after which Animal was Kept Alive.*

1. Removal of one complete cerebral hemisphere in 40 cats.
2. Removal of motor area only in 4 cats.
3. Division of the crus cerebri in 2 cats.
4. Removal of a lobe of the cerebellum in 10 cats.
5. Hemisection of the spinal cord in 4 cats.
6. Complete section of the spinal cord in 2 cats.

II. *Lesions after which Animals were not Kept Alive for any Length of Time.*

1. The preceding operations.
2. Removal of both cerebral hemispheres.
3. Removal of the cerebellum.
4. Removal of one cerebral hemisphere and opposite lobe of cerebellum and *vice versâ*.
5. Removal of one hemisphere and division of opposite half of the spinal cord.

Where the animals have been kept alive, the symptoms during life and the anatomical changes found after death have been investigated, and in all cases the results of absinthe stimulation have been recorded by the graphic method.

In order to enable a clearer comparison to be made between the various results obtained by the experimental and anatomical methods, the paper is divided into—

I. The anatomical changes.
II. Behaviour of the animal during life.
III. Results of absinthe stimulation.
IV. Conclusions.

## Part I.—*Anatomical Changes.*

The investigations of the degenerations have been made in every instance by the Marchi method upon animals which have been kept alive from a few days to three months.

### *Removal of one Cerebral Hemisphere (Left), or complete Section of the Left Crus Cerebri flush with the Tentorium.*

The results of these lesions as regards the descending degenerations are identical.

They show that in the higher bulbo-spinal segments, from the 3rd nerve downwards, there exist long descending internuncial fibres, which are grouped anteriorly and laterally as in the spinal cord; in other words, that the anterior, antero-lateral, and lateral columns of the cord can be traced from the level of the superior corpora quadrigemina.

*Anterior Columnar Fibres.*—These fibres begin to group at the level of the uppermost part of the 3rd nerve against the anterior and inner aspect of the grey matter of the aqueduct of Sylvius; they constitute the commencement of the posterior-longitudinal bundle. The degenerate fibres are absolutely limited to the side of the lesion; they occupy, for the most part, the inner portion of the posterior-longitudinal bundle, and they can be traced to the end of the cervical spinal cord. The higher the lesion the fewer are the number of degenerate fibres in the post.-longitudinal bundles; if the lesion extends much below the 3rd nerve, the degeneration of the post.-longitudinal bundle is very complete. New fibres are continually being added to the post.-longitudinal bundle in its passage through the bulbar segments, the degenerate fibres in consequence moving more anteriorly. In the spinal cord the degenerate fibres are scattered through the middle and post.-thirds of the anterior column on its inner aspect and closely simulate a direct pyramidal tract.

*Antero-lateral Columnar Fibres.—Meynert's fibres* (fountain decussation) pass from the side of the lesion across the raphe immediately ventral to the post.-longitudinal bundles, and turn vertically down, lying in the raphe in front of the post.-longitudinal bundles. The fibres can be traced into the antero-lateral column of the cord as far as the lower cervical region. In their descent they move slightly forwards, but they are always more anterior than the fibres of the post.-longitudinal bundles. The degeneration method shows that Meynert's fibres arise in a focus close to the point of commencement of the descending root of the 5th, on a level *with the roots* of the 3rd nerves. The vast majority of the fibres decussate completely; the decussation is a very horizontal one.

*Lateral Columnar Fibres.*—In the highest segments these are derived from fibres, which decussate in front of the preceding group, and originate from a slightly higher level in the tegmentum; they probably correspond to Forel's decussating fountain fibres. In the mesencephalon they occupy a position in front of and slightly external to the antero-lateral columnar fibres; lower down they are more laterally situated, and in the pons and medulla form a well defined group, immediately in front of the ascending root of the 5th and the substantia gelatinosa, and dorsal to the nucleus lateralis; they are traversed by the root of the 7th, and are bounded externally by trapezoid, and ascending cerebellar fibres. They are internal to the lemniscus and quite distinct from it; they can be traced to the upper lumbar spinal cord. In the spinal cord they occupy a position immediately in front and to the outer side of the pyramidal tract; they are readily distinguished from the latter by their large size.

*Degeneration of Descending Root of 5th.*—The Marchi method shows that this root is invariably degenerate upon the side of the lesion. It arises in the lateral aspect of the Sylvian grey matter at about the level of the upper oculo-motor nucleus, descends to meet the ascending root, and passes out without interruption.

*Pyramidal System.*—The degeneration is confined exclusively to the pyramid on the side of the lesion, and the degeneration appears complete.

There is a slight *bifurcation* at the decussation, a small group of fibres passing back to the lateral tract on the same side. There is thus a *direct lateral pyramidal tract*, but there is no *anterior* direct pyramidal tract.

The decussation of the pyramid is not confined to the cervical region; degenerate fibres leave the pyramidal system from the internal capsule, the crusta, and from the pyramid in the medulla. A large group passes through the thalamus and beneath the corpora quadrigemina, many of the fibres crossing over in the roof of the aqueduct. A considerable number of degenerate fibres pass back to

the quadrigeminal region from the outer and dorsal part of the crusta.

In the *posterior commissure*, *pineal commissure*, and *corpus callosum* there are numerous degenerate fibres.

When the motor area or anterior third of the brain is removed, the degeneration is confined to the pyramidal system, the contrast with the results of hemisection of the mesencephalon being, therefore, very striking.

Comparing hemisection of the mesencephalon with hemisection of the cord, the difference, as regards the internuncial fibres, is the greater amount of decussation in the mesencephalon than in the cord. The internuncial fibres are conspicuous by their large size.

Comparison with ascending degenerations at the various levels shows that the descending tracts described above are distinct from the ascending.

*Lesion of the Cerebellum.*—When one lobe of the cerebellum is removed there is degeneration of the superior cerebellar peduncle. I have found no evidence of the descending columnar degeneration described by Marchi.

## Part II.—*Symptoms of Animals during Life.*

Comparing the relationship between the extent of the degenerations and the symptoms, it is found that—

Removal of the motor area entails degeneration of the pyramid alone, and a temporary paresis; the animal appearing, after a short time, quite like the normal.

Removal of a cerebral hemisphere or hemisection in the quadrigeminal region gives rise to degeneration of the pyramidal and internuncial systems and fibres. The symptoms are more pronounced; sensation is much altered; there is great difficulty of feeding.

Hemisection of the cervical spinal cord produces extensive degeneration of the anterior and lateral columns of the cord. There is at first hemiplegia, the vasomotor disturbance is much greater, and the sensory and motor paresis lasts longer.

Removal of a lobe of the cerebellum does not appear to be accompanied by descending columnar degeneration; the symptoms may be very slight, or there may be incoordination and sensory and motor weakness upon the side of the lesion. The manifestation of the motor weakness differs from that seen in the cats, in which the pyramid is degenerate. There is no wrist drop in the cerebellar cat. The weakness in the case of the pyramidal cats is uncomplicated; on the contrary, that in the cerebellar cat is intimately bound up with complex phenomena of incoordination.

The evidence would tend to show that the weakness in the two cases is due to different causes.

## Part III.—*Results of Absinthe Stimulation.*

The absinthe has been injected either immediately after the operation or after complete recovery. There are, therefore, two categories of experiments, viz., "immediate" and "remote"; but, as a rule, the difference between the average results in both cases is slight. The fit was registered by spring myographs attached to the extensor tendons of the fore paws.

### 1. *Removal of one Cerebral Hemisphere, or Hemisection of the Mesencephalon, and Immediate or Remote Absinthe Stimulation.*

*Result.*—There are bilateral fits. On the paretic side the initial fit may be much smaller than on the left side; in the subsequent fits, tonus is more marked than clonus; the final clonic contractions are less numerous.

### 2. *Removal of Left Motor Area; Immediate and Remote Stimulation.*

*Result.*—The fits upon the right and left sides more closely resemble one another; there is considerable clonus upon the "paretic" side as well as upon the normal.

### 3. *Removal of both Hemispheres.*

*Result.*—Immediate removal of the hemispheres arrests the fits; a slight respiratory response can, however, be elicited. Where one hemisphere has been first removed, and after recovery the remaining hemisphere and absinthe has been given, contractions have been obtained, occurring at regular intervals and equal upon both sides; in one case the contraction was most marked upon the side corresponding to the hemisphere first removed. Removal of both hemispheres and stimulation upon the second day was followed by two strong fits, made up of a series of contractions following one another fairly rapidly, but not so rapidly as in the clonus when a hemisphere is present.

Where both motor areas have been removed in succession, regular tonic and clonic bilateral responses have been obtained; the rhythm of the clonus is much slower than when the cortex is intact.

4. *Removal of Cerebellum and Immediate Absinthe Stimulation. Removal of one Lobe of the Cerebellum. Removal of Left Hemisphere and Left Lobe of the Cerebellum. Removal of Left Hemisphere and Right Lobe of the Cerebellum and v. v. Immediate and Remote Absinthe Stimulation.*

*Result.*—Removal of the whole cerebellum does not stop the fits, nor impart to them any special character. Removal of one lobe of the cerebellum appears to have very little effect upon the fits. Where, in addition the opposite cerebral hemisphere is removed, the fits appear similar to those seen when the hemisphere alone is removed.

5. *Removal of Left Hemisphere and Subsequent Section of the Right and Left Halves of the Cervical Spinal Cord.*

*Result.*—Conduction abolished on the side of section.

6. *Hemisection of the Upper Cervical Spinal Cord and Absinthe Stimulation.*

*Result.*—In cats which have partially recovered from the effects of the hemisection, absinthe produces a response upon the side which was divided.

7. *Complete Section in the Dorsal Region.*

*Result.*—In two cases of complete recovery (complete paralysis of the hind quarters remaining), absinthe did not elicit a response from the distal segment of the cord; the experiments, however, require repeating.

## Part IV.—*Conclusions.*

The formation of the descending system of the anterior, antero-lateral, and lateral columns can be seen in the mesencephalon.

There is a marked decussation of the lateral and antero-lateral column fibres in the mesencephalon. The anterior column fibres (post.-longitudinal bundle) appear to be direct fibres. Decussation is, however, not limited to this region; it occurs in the spinal cord, and probably throughout the bulbo-spinal system.

Decussation of the pyramidal system is not limited to the cervical region; it occurs in the higher segments. As in the preceding system so in this, there is a direct path—the direct lateral pyramidal tract, and there is evidence of direct fibres in the higher segments.

There is bilateral distribution of both systems of fibres, but there is no evidence whatever of recrossed fibres.

No fibres get into the opposite pyramid by way of the corpus callosum.

Stimulation with absinthe shows that the bulbo-spinal centres (including the cerebellum) alone, can produce a series of clonic fits, differing from the cortical in the much slower rhythm of the contractions. But from the complete section of the cord experiments it seems improbable that the cord alone can be excited by absinthe.

Immediate hemisection of the cord prevents the absinthe fit on that side; but after recovery a modified fit results upon the side of the lesion, in spite of the fact that the direct lateral and crossed pyramidal tracts are completely degenerate, as well as the internuncial fibres in the anterior and lateral columns.

When one hemisphere is removed or a complete hemisection made in the quadrigeminal region, there are bilateral fits, in spite of the fact that one pyramidal system is completely degenerate. The fits are modified upon the side opposite to the lesion, the clonus being less marked, and the first fit being absent or very small.

If, in the last two cases, a hemisection is made upon the side of the degenerate pyramid, it instantly arrests the fits upon that side, the section interrupting the sound direct pyramidal tract.

I therefore conclude that the maximal effect of absinthe is produced when the motor area is present, and that the impulses generated there are distributed by the pyramidal system in the way described, the maximal effect crossing to the opposite side, the question of unilaterality or bilaterality being one of degree as shown by the differences between the initial and subsequent fits, and as borne out by the relative sizes of the crossed and uncrossed tracts.

The epilepsy due to absinthe indicates that there are probably very many epileptiform attacks in man which are toxic.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*From the Journal of Physiology. Vol. XVI. Nos.* 1 *&* 2, 1894.]

# NOTE ON THE DEGENERATIONS OF THE ROOTS OF THE Vth NERVE.

By RUBERT BOYCE, M.B., *Assistant Professor of Pathology, University College, London.*

(Plate VII.)

(*From Pathological Laboratory, University College, London.*)

In the course of some observations in the cat with regard to degeneration resulting from removal of one hemisphere and from hemisection in the mesencephalon in the quadrigeminal region, I have invariably found descending degeneration of the descending root of the Vth, as shown by the Marchi method. In two of the very large series of cases examined, there was however in addition degeneration of the ascending root.

*Descending root of* V*th.* The cords were furnished by animals which lived from ten days to three months after the operation. The degeneration of the root was limited without exception to the side of the lesion. The opposite nerve was free from degeneration. In every case the origin of the nerve was implicated in the wound, which was with very rare exceptions strictly unilateral and did not extend downwards. The degenerate trunk which is very large, descends towards the level of the nucleus of the VIIth, curves downwards and sweeps out in bundles which ascend and join in with the anterior and inner portion of the ascending root (Fig. 1); the lowermost bundle is very closely applied to the root of the VIIth. Owing to the looping, the root will at a certain level be cut twice, both whilst it is descending and ascending. I find, as is stated, that the root originates in the lateral portion of the Sylvian grey matter, behind the large oculo-motor nucleus, its highest part coming into relationship with the upper oculo-motor nucleus. As the degenerate trunk descends, new fibres come into it which originate in all probability in the grey matter on

its inner aspect; these fibres are not degenerate, not having been involved in the lesion, but whether they run out in the Vth or in the VIIth, I have not as yet been able to determine, the two nerves being so very close together. In harmony with these facts I have noted that the total amount of degeneration in the descending trunk may vary; thus in one case where the lesion penetrated into the upper part of the pons, the trunk was completely degenerate, whilst in the other more usual cases, where the lesion only extended to the oculo-motor level, the trunk lower down contained healthy fibres. From their origin to their exit the fibres have an unbroken course.

*Ascending root of* V*th.* In the two cases in which degeneration was observed in the ascending root, the lesions which produced the degeneration were accidental, and were sequelæ to the operation of removal of the hemisphere, which had been made a few weeks previously. In both cases there was evidence of the extension of the wound downwards into the pons, and in one of the cases a granuloma was present at the level of entry of the nerve in the middle of the pons. Sections at lower levels showed an absence of inflammatory reaction. As the Figs. 2 and 3 show, the degeneration in the ascending root is scattered and is not complete. The degenerate fibres diminish in numbers as the tract is traced downwards and there is evidence in many of the sections that the fibres turn into the substantia gelatinosa. The fact that in each of the above cases, the degeneration diminished downwards and that there was evidence of inflammatory reaction at the level of entry of the nerve, points that the degeneration is an ascending one and accords with embryological facts.

Experimental observations upon the degeneration of the ascending root are very few, and in many of these cases the root was cut low down in the medulla. I refer to Vulpian, Herzen and Loewenthal, Tooth, Sherrington and especially to Forel who extirpated the ganglion in the young rabbit and obtained very complete atrophy of both the ascending root and the substantia gelatinosa. Most recently Ferrier and Turner describe injury to the ascending root followed by its degeneration to the 2nd cervical; they also note atrophy (not degeneration) of the descending root above the lesion of the lower end of the trunk in their cerebellar operations.

My observations lead me to believe that the descending efferent system of the Vth is part of the efferent system of higher segments, that it is in fact a middle root as advocated on morphological grounds by Gaskell.

I do not propose to discuss here the central connections of the nuclei of the Vth nerve, but I may mention that in the great majority of my experiments the fillet was completely divided in the mesencephalon (the animals killed ten days to three months after the operation) and that I have not found any degeneration or atrophy which supports Hösel's view of the connection of the fillet fibres with the sensory nucleus of the Vth.

## PLATE VII.

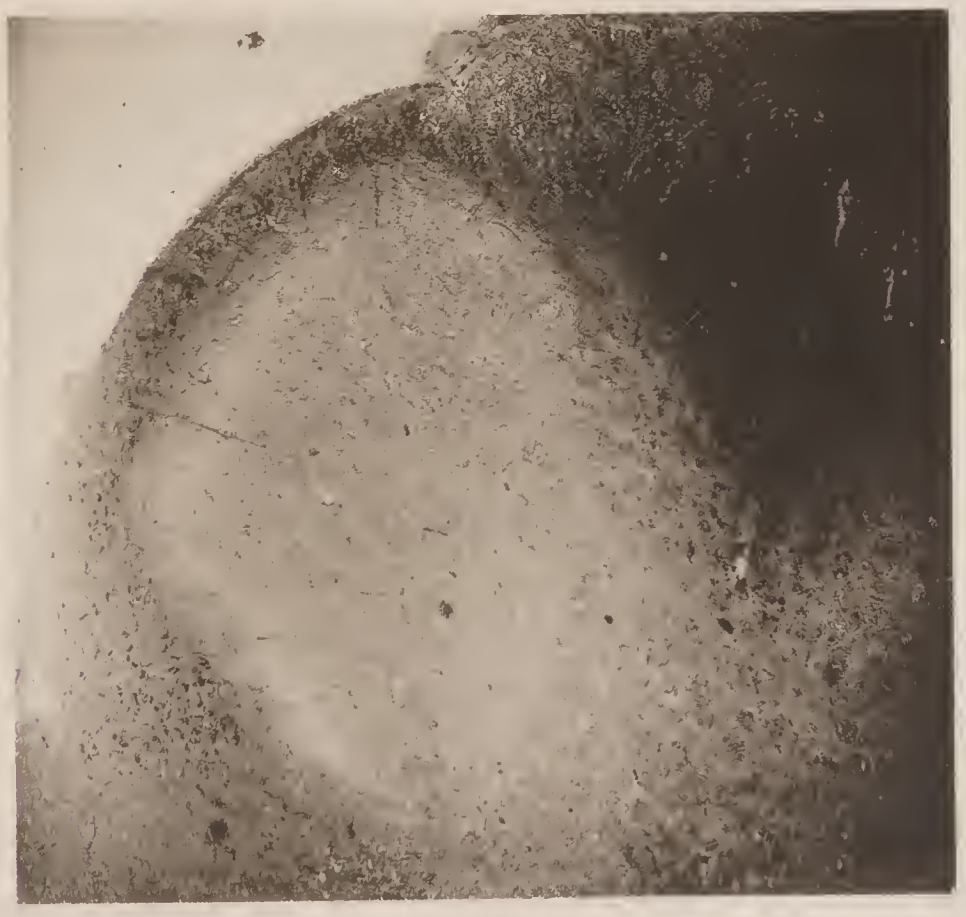
Fig. 1. Section through pons at level of entry and exit of ascending and descending root of Vth. The descending root-fibres (degenerated and cut obliquely) are sweeping out in bundles and occupy the anterior and inner part of the nerve trunk. The ascending root is normal. Cat, hemi-section of mesencephalon (quadrigeminal region). Obj. 35 mm.

Fig. 2. Section through lowest part of pons. There is considerable degeneration of the ascending root of Vth. It is bounded by the VIIth and VIIIth nerves. Cat, injury in lower part of pons. Obj. 35 mm.

Fig. 3. Section through lower portion of medulla. The degenerate fibres of the ascending root surround the substantia gelatinosa externally and slightly posteriorly. The degenerate fibres to the inner and anterior aspect of the substantia are direct lateral quadrigeminal fibres. Cat, as in fig. 2.

I.

II.



III.

[*From the* Proceedings of the Royal Society, Vol. 55 ]

# "On the Effects produced on the Circulation and Respiration by Gunshot Injuries of the Cerebral Hemispheres."

By S. P. Kramer, M.D., and Victor Horsley, M.B., F.R.C.S., F.R.S., Professor of Pathology in University College, London. Received February 21, 1894.

(From the Laboratory of the Pathological Department, University College, London.)

(Abstract.)

In consequence of the fact that the effects produced on the circulation and respiration by a bullet passing through the cerebral hemispheres are but little understood, the authors instituted a series of pathological experiments on etherised dogs, and of physical experiments on various substances.

The results obtained establish, beyond question, that the primary cause of death under these circumstances is not, as is usually supposed, due to failure of the heart, but to arrest of the respiratory movements. Further, the authors have found, in confirmation of this, that death can be prevented by the employment of artificial respiration, except under certain circumstances detailed in the paper.

After describing the changes in the circulation produced, and which consist of (*a*) slight initial fall of blood pressure, (*b*) considerable later rise of blood pressure, (*c*) preservation of the rhythm of the heart, the authors discuss the physical effects of the projectile on the encephalic contents, and they show, as was originally contended by Professor Kocher, that the action of the bullet is essentially a hydrodynamic one, and that it is the lateral pressures which cause mechanical lesion of the respiratory centre.

In this respect the results obtained further support the original observations of Spencer and Horsley, recently confirmed by Hill, viz., that the respiratory centre is the first to be seriously affected by changes in the intra-cranial tension.

Finally the authors point out that, supervening on the primary arrest of respiration, there ensues a gradual rise in the intra-cranial tension due to the hæmorrhage within the skull cavity, and that the phenomena which then follow are the same as those described in the above-mentioned paper.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*From the* Proceedings of the Royal Society, Vol. 55.]

# "A Research into the Elasticity of the Living Brain, and the Conditions governing the Recovery of the Brain after Compression for Short Periods." By A. G. Levy, M.B. (London). Communicated by Professor Horsley, F.R.S. Received February 21, 1894.

(From the Laboratory of the Pathological Department of University College, London.)

(Abstract.)

(Towards the expenses of this research a grant was made by the British Medical Association at the recommendation of the Scientific Grants Committee.)

In view of the great frequency of compression of the brain as a pathological condition, it seems very advisable to attempt to obtain some knowledge of the elementary factors conditioning the physical changes in the brain substance due to mechanical pressure.

Grashey* has already definitely proved that the coefficient of compressibility of the dead brain is slightly less than that of water, which is equivalent to saying that under any ordinary pathological conditions the brain tissue is incompressible. At the suggestion of Professor V. Horsley, who devised an apparatus for the purpose, and to whom I am indebted for advice and suggestions, an attempt was made to determine the elasticity of the living brain, *i.e.*, of the brain mass with its full complement of circulating blood and lymph, and further to test the truth of the generally accepted view that the elasticity of the brain is proportional to the blood pressure.

The brain was experimented upon *in situ*, the influence of the cerebro-spinal fluid being excluded by the mere fact of the skull being opened and the membranes partially reflected, thus releasing the fluid from all tension. Thus we arrive at the properties of the brain mass itself as it rests upon its osseous enclosure.

There were, in the first place, considered the results of experiments

* Grashey, "Ueber Hirndruck und Hirncompression." 'Allg. Ztschr. f. Psychiat.,' Berlin, 1887, vol. 43.

performed upon freshly-exposed brains, the blood pressure being at its normal height, in order to arrive at some conclusion as to the normal elasticity of the brain. The downward movement of a plunger was measured after a given interval of time, and the extent of this is termed the "excursion." The recovery of the brain surface, to the extent of which the term "recoil" is applied, was measured until it failed to perceptibly develop further. The general character of the excursion is that of a rapid plunge downwards taking place within the space of one or two seconds, followed by a much more gradual compression. Its extent varies within a considerable range in different animals; thus a weight of 50 grams applied for one minute produces an excursion which varies in different dogs from 4·5 to 7·3 mm. It also varies notably with the weight employed. There is no obvious relation between the depth of excursion and the blood pressure.

For convenience of expression and of comparison the ratio of the excursion to the recoil is in the full paper expressed in the form of a fraction, and this ratio is termed the "proportionate recoil;" the smaller this fraction the feebler the elastic reaction it denotes, and *vice-versâ*. A comparison of the ratios derived from experiments performed under like conditions upon different animals brings out the striking approximation which they bear to one another, whatever the length of the excursion and whatever the existing blood pressure may be. And such deviations from the average as the ratios present cannot be found to have any relation to variations in either excursion or blood pressure. A compression by a 50-gram weight for a period of from 30 seconds to one minute yields an average proportionate recoil of $\frac{1}{2}$. A further comparison definitely shows that the longer the period of compression the less is the recoil; thus with a compression of only two seconds the reaction is sometimes almost perfect, whereas a compression lasting six miuutes yields a ratio of 1/2·74. Heavier weights similarly damage the brain in a fashion prejudicial to its recovery.

A series of experiments were performed with a view to comparing the "elasticity" of the brain at the normal blood pressure with the "elasticity" of the same brain at an artificially lowered blood pressure. The first method employed was that of producing a large fall of blood pressure by bleeding. The results tended to confirm the impression that there exists no constant relation between brain elasticity and blood pressure. This series is somewhat vitiated by the partial collapse of the cerebrum which ensues during the process of bleeding, and a second series was instituted, in which the blood pressure was lowered through the agency of amyl nitrite; the brain at the moment of administration becoming flushed with blood, it has no tendency to collapse. Under the influence of this drug the cerebral vascular con-

ditions are such that the "elasticity" is actually increased, thus conclusively demonstrating the non-dependence of the latter upon the central arterial pressure.

A further series of experiments were performed in view of the influence which venous pressure is believed to exert upon the cerebral circulation. This object was carried out by exposing the accessible cranial veins and clamping them in succession, and by measuring the variation in the intra-cranial pressure induced by this means. The results tended to show that the increase of intra-cranial pressure must be considerable to influence the "elasticity" in even a small degree.

Experiments performed upon brains which had undergone prolonged or severe compression showed that a considerable increase of arterial blood pressure is quite unable to restore the volume of the brain thus damaged, whereas an increase of venous pressure, obtained by asphyxiation, rapidly, and usually completely, brings this about.

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[*From the* Proceedings of the Royal Society, Vol. 55.]

# "Preliminary Note on Bilateral Degeneration in the Spinal Cord of Monkeys (*Macacus sinicus*) following Unilateral Lesion of the Cortex Cerebri."

By E. L. Mellus, M.D. Communicated by Professor V. Horsley, F.R.S. Received December 22, 1893.

(From the Pathological Laboratory of University College, London.)

Having for some time been engaged in an investigation of the question as to how far the fibres of each pyramid descend both halves of the spinal cord, I am in a position to state that in the bonnet monkey (*Macacus sinicus*) the following arrangement prevails.

*Method of Investigation.*—The animal being etherised, and the left hemisphere of the brain exposed by a single trephine hole (sometimes enlarged afterwards), a small portion of the excitable area of the motor cortex was selected as detailed below, the selection being confirmed in each case by electrical stimulation. A small piece of the cortex, about 0·4 cm. square, constituting the focus of the movement observed, was removed, care being taken to remove also a little of the underlying corona radiata to be sure that no cortex was left. The wounds healed, without exception, within 24 hours by first intention. Beyond slight paresis, which generally disappeared in 24 hours, no symptoms were observed to result from the excision. Professor Horsley kindly did the operations for me. After three weeks the animals were killed, the brain and cord hardened in Müller's solution, and stained in osmic acid after the method of Marchi.

*Results of Investigations.*

Three foci of representation were selected for excision, the left hemisphere being chosen in every case (*vide* Method of Investigation).

I. Focus for the movements of the thumb.
II. Focus for the movements of the hallux.

The course taken by the descending degenerated fibres was as follows:—

I. *Hallux Focus removed.*—In this case the lesion consisted of the removal of about 16 sq. mm. of cortex between the superior precentral sulcus and the fissure of Rolando, and bounded below by the level of the superior frontal sulcus.

Degenerated fibres were found in both lateral columns of the cord, the large majority being on the right side. The degenerated fibres were scattered throughout the entire area of the crossed or lateral pyramidal tract, not being restricted to any special part of it, though it might be said they were a little more dense posteriorly. Throughout the cervical, dorsal, and lumbar regions the total number of degenerated fibres was not diminished, though, of course, relatively increased in the lower cord. In the pons and medulla the degeneration was entirely confined to the left pyramidal tract (the side of the lesion). At the decussation in the upper cervical region the degenerated tract divided; about one-third going to the lateral column of the same side, the remaining two-thirds crossing to the lateral tract on the opposite side. In the upper cervical region there were a very few degenerated fibres remaining in the direct tract (anterior column), and below the middle of the cervical enlargement none could be seen.

II. *Thumb Focus removed.*—In this case the lesion consisted of a similar removal of cortex at a point just above the lower end of the intra-parietal sulcus, and between it and the fissure of Rolando, and, consequently, just behind the inferior genu of the fissure of Rolando (Beevor and Horsley). As in the case of the hallux focus, degeneration was also confined to the pyramidal tracts of the same side (left) as the lesion, throughout the pons and medulla. At the decussation of the pyramids there was also a slight division of the degenerated fibres, but in this case a few fibres only (less than one in ten) went to the lateral column of the same (left) side of the cord. There may have been two or three degenerated fibres left in the direct tract after the decussation, but this could not be positively stated. In the cervical and upper dorsal regions the degenerated fibres gradually decreased in number. At the level of the second dorsal there were a very few degenerated fibres still left in each lateral column. At the third dorsal they had entirely disappeared.

It seems probable, from these observations, that a second decussation lower down in the cord—recrossing—does not occur, and that the bi-lateral degeneration observed by Pitres, Sherrington, Langley, Muratoff, and others is a genuine bi-lateral descent of fibres from one hemisphere.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*From the* Proceedings of the Royal Society, Vol. 55.]

# "Experimental Researches into the Functions of the Cerebellum."

By J. S. Risien Russell, M.D., M.R.C.P., Assistant Physician to the Metropolitan Hospital. Communicated by Professor Victor Horsley, F.R.S. Received December 14, 1893.

(From the Pathological Laboratory of University College, London.)

(Abstract.)

The views that have been expressed as to the probable functions of the cerebellum are briefly alluded to, and the results obtained by previous investigators, as the direct outcome of experimentation, are detailed at greater length.

The objects of the present research were to determine :

1. Whether each lateral half of the cerebellum is capable of acting independently, or whether it is necessary for the connexions between the two halves to be intact, in order that the functions of the organ should be properly performed.

2. If impulses pass from one side of the organ to the other before they are transmitted to the cerebrum or spinal cord.

3. What is the nature of the impairment of movement which results when portions of the organ are removed.

4. What relationship exists between one half of the cerebellum

and the cerebral hemisphere of the opposite side, and what is its probable nature.

5. Whether one lateral half of the cerebellum is related mainly to the same side of the spinal cord, to the opposite side, or to both, and what the nature of the relationship is.

6. What symptoms resulting from experimental lesions of the cerebellum are mostly to be relied on for localisation.

7. Whether any, and if so which, of the symptoms are dependent on interference with the labyrinth or 8th nerve when experimental lesions of the cerebellum are produced.

The procedures adopted in attempting to elucidate these problems were :

1. Median vertical section separating the two lateral halves of the cerebellum from each other.

2. Extirpation of one lateral lobe.

3. Removal of half the organ, *i.e.*, of one lateral lobe together with one lateral half of the middle lobe.

4. One or other of the last two methods of procedure as a preliminary, and subsequent comparative investigation of the excitability of the two cerebral hemispheres.

5. Similar preliminary methods as in the last instance, followed by the administration of the essential oil of absinthe, and comparison of the effect of the resulting convulsions on the muscles of the two sides of the body.

6. Removal of both lateral lobes of the cerebellum.

7. Extirpation of the whole or half of the posterior part of the middle lobe.

8. Ablation of the whole organ.

9. Control experiments on the labyrinth and 8th nerve, which consisted in :

(*a*) Extirpation of the labyrinth.
(*b*) Intracranial section of the auditory nerve.
(*c*) Chemical irritation of the auditory nerve

The results detailed refer chiefly to dogs, but the effects of similar lesions of the cerebellum in monkeys are contrasted with these. The question as to whether the cerebellum exerts any trophic influence is separately considered, as is a case of defective development of the cerebellum in a cat.

The investigation of the excitability of the two cerebral hemispheres, as tested by the induced current, yielded results of more than ordinary interest, for, whereas the excitability was equal on the two sides when the cerebellum was intact, the opposite hemisphere was the most excitable after unilateral ablation of the cerebellum, which difference in the excitability persisted, and was still present

even three months after the half of the cerebellum had been removed. The results obtained when absinthe was administered to animals which had been deprived of half the cerebellum also yielded highly interesting and instructive results. The increased excitability of the opposite hemisphere was evidenced by the exaggeration of the convulsions on the side of the cerebellar lesion; and it became also evident that the convulsions on the opposite side were diminished. Further, the curves obtained from the extensor muscles of the anterior extremity on the side of the cerebellar lesion showed that there was a marked alteration in the second stage of the convulsive seizure, for the tonus characteristic of this stage of similar convulsions evoked in dogs whose central nervous system was intact was either replaced by clonic spasms, or a large element of clonus was superimposed on the tonus. The curves from the muscles of both anterior extremities showed this alteration in the second stage of the convulsions when the whole instead of the half of the cerebellum had been previously removed.

The chief conclusions which appear to be warranted are that the one half of the cerebellum does not, in any great measure, depend on the cooperation of the other half for the proper performance of its functions. The bulk of the impulses pass from one half of the organ to the cerebrum, or spinal cord, without passing to the other half. Three factors are responsible for the defective movements which result on ablation of different parts of the organ—incoordination, rigidity, and motor paresis. The last of these is probably directly due to the withdrawal of the cerebellar influence from the muscles, while the exalted excitability of the opposite cortex cerebri, which results after unilateral ablation of the cerebellum, is probably a provision for compensation in this and other connexions. The one half of the cerebellum controls the cells of the cortex of the opposite cerebral hemisphere, and those of the anterior horns of the spinal cord on the same side chiefly, and on the opposite side to a slight extent. It is further suggested that either the cerebral hemisphere whose excitability is increased inhibits the opposite hemisphere, or that, under normal conditions, one half of the cerebellum inhibits the other half, which inhibition being no longer operative, owing to ablation of half of the organ, allows the remaining half to exert an increased control on the opposite cortex cerebri, or on the spinal centres of the same side, or possibly in both directions; but which is the most probable explanation of the phenomena observed is at present left an open question.

The symptoms characteristic of unilateral ablation of the cerebellum are:

1. Rotation and reeling to the opposite side.
2. The side of the face corresponding to the side of the lesion is

directed up, and the spinal column is arched with its concavity to the side of the lesion.

3. Incoordination, chiefly in the limbs of the same side.

4. Rigidity, most marked in the extremities of the side of the lesion, and preponderating in the anterior extremity of the side.

5. Exaggeration of the tendon reflexes most marked on the same side.

6. Motor paresis affecting both extremities on the side of the lesion, and the posterior extremity of the opposite side.

7. Anæsthesia and analgesia having the same distribution as the motor paresis.

8. Deviation of the opposite eyeball downwards and outwards, while that of the same side, if deviated, looks upwards and to the side of the lesion.

9. Lateral nystagmus, the jerks being from the opposite side towards the side of the lesion.

The phenomena which characterise ablation of different parts of the middle lobe, and of the whole organ, are similarly described. Incoordination is next discussed, and it is urged that, instead of looking on the cerebellum as a distinct organ which has a special function, distinct from those subserved by other parts of the central nervous system, it would be more correct to look on it as a part of that system, having many functions in common with other parts of it, the chief difference between one part of this great system and another being the degree in which different functions are represented in any given part: *e.g.*, with regard to motor power, the anterior extremity is maximally represented in the cerebrum and minimally in the cerebellum, whereas the trunk muscles are minimally represented in the cerebrum and maximally in the cerebellum. Arguments are adduced in favour of looking on the ocular deviations which result from ablation of parts of the cerebellum as paralytic rather than irritative phenomena, and two forms of nystagmus are recognised as consequent on cerebellar lesions, one which is spontaneous, and the other which is only evoked on voluntary movements of the globes, and the probable difference in their ætiology discussed. Finally, the phenomena characteristic of unilateral ablation of the cerebellum are contrasted with those the result of extirpation of the labyrinth, and it is shown that no single phenomenon is the same in the two.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

"The Effect produced upon Respiration by Faradic Excitation of the Cerebrum in the Monkey, Dog, Cat, and Rabbit." By W. G. Spencer, M.S., M.B., Assistant Surgeon to the Westminster Hospital. Communicated by Professor Victor Horsley, F.R.S. Received December, 15th, 1893.

(From the Pathological Laboratory of University College, London.)*

(Abstract.)

The author of the paper brings forward evidence to show that whilst the effect upon respiration of exciting the cerebrum in a non-anæsthetised animal is probably a complex one, yet, by careful regulation of the anæsthetic state, four constant effects can be obtained upon respiration by stimulation of the cortex, and these can be traced down, each in a course of its own, from the cortex to the medulla oblongata. In the production of the anæsthetic state, the author lays stress not only upon the drug (ether) used, but also upon the following general conditions—apnœa, loss of blood, exposure of the brain, extravasation of blood, general exhaustion of the animal, and departure from health prior to the experiment.

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* Grants have been made towards the research by the Royal Society and by the British Medical Association.

The four effects upon respiration obtained in this research are as follows :—

A. *Diminution of Action.*

*Slowing and Arrest of the Respiratory Rhythm.*—The cortical area where this result was obtained is situated just outside the olfactory tract in front of the point where the tract joins the temporo-sphenoidal lobe. On exposing successive and vertical sectional surfaces of the hemisphere the same result was obtained by exciting in the line of the strand of fibres known as the olfactory limb of the anterior commissure. After decussating at the anterior commissure, the tract is continued backwards on either side of the infundibulum into the red nucleus below and external to the aqueduct at the plane of exit of the third nerve.

B. *Increased Action.*

1. *Accleration.*—Commencing from a point on the convex surface, of the cortex within the "sensori-motor" area, the effect may be followed back just below the lenticular nucleus where it borders on the outer and ventral portion of the internal capsule; the strand runs at first external and then ventral to the motor portion of the internal capsule, and so reaches the tegmentum. The lines from the two sides meet in the interpeduncular grey matter at the level of and just behind the exit of the third nerve.

2. *Hyperinspiratory Clonus* ("snuffing movements").—This effect was obtained by excitation at the junction of the olfactory bulb and tract, and then carrying the stimulation backwards along the olfactory tract; the same result was found when the uncinate convolution of the temporo-sphenoidal lobe was irritated. Followed from the uncus, this excitable region passed behind the optic tract to the crus, and then lay ventrally to the crusta. The excitable tract on each side thus converged towards the middle line at the upper border of the pons.

3. *Hyperinspiratory Tonus.*—This experimental result is of such frequency and constancy as to be clearly an important general phenomenon. It can be elicited in various ways, *e.g.*, excitation of the descending motor tract in the corona radiata and internal capsule yielded this result; so did excitation of the fifth nerve and dura mater, as well as the sciatic nerve, both before and after complete removal of the cerebrum at the tentorium cerebelli.

The author finds medullated fibres in prepared microscopical vertical (frontal) sections of the brain running in the same course as that indicated by faradic excitation of the living surface of the section of the hemisphere. For his conclusions he has relied solely upon tracings of the respiratory movements. Fifty-six tracings are included as illustrations, together with thirty photographs of brains and brain sections to show the precise points excited. The author records his thanks to Mr. Horsley for help, and to Dr. Howard Tooth for the loan of excellently-prepared sections.

[*From the* PROCEEDINGS OF THE ROYAL SOCIETY, Vol. 54.]

# "Some of the Effects and Chemical Changes of Sugar injected into a Vein."

By VAUGHAN HARLEY, M.D., Teacher of Chemical Pathology, University College, London, Grocer Research Scholar. Communicated by GEORGE HARLEY, M.D., F.R.S. Received June 13, 1893.

(From the Physiological Institute, Leipzig.)

It being no longer doubted that sugar is essential to life, and it having been experimentally shown that the animal organism can form saccharine matter out of proteids, as well as carbohydrates, it becomes of importance to know what changes sugar undergoes in the body before its elements are finally eliminated.

According to present knowledge, it is considered that by the three chemical processes of hydration, oxidation, and reduction, the molecule of sugar is changed into larger and smaller molecular groups, and that it is in the breaking down and building up of these that heat and vital energy are developed. The basis of this belief rests on the observation that when sugar is artificially introduced into the

system its disappearance is accompanied by the liberation of heat and the development of muscular energy.

To discover the *modus operandi* of this is a matter of extreme difficulty, from the fact that when sugar is artificially introduced into the living circulation it is rapidly distributed to every organ of the body. In each of these it undergoes specific changes. So that, while the number of its derivatives are great, the amount of each is proportionally small. So small is it, indeed, of some of them, as to render their collection in sufficient quantity for the purposes of investigation next to impossible. However, by the advice and kind assistance of Professor C. Ludwig, I made the attempt, and the present communication, which I have the honour to lay before the Royal Society, embodies in brief the results of the research.

The methods adopted were briefly as follows:—As sugar artificially introduced into the veins is rapidly, and in different animals in varying proportions, eliminated by the kidneys, the ureters were ligatured so as to retain the sugar in the organism. In all cases where it was intended to kill the dogs within a few hours, the ligaturing was done from the front. Whereas, when it was intended to keep the dog alive, the operation was performed from behind, and the ureters tied by means of a ligature-staff, so that, at any given time, the ligatures could be removed without re-opening the wound. In order that all the animals should be under exactly the same conditions, in so far as their assimilative functions were concerned, no food was given to them during the previous twenty-four hours.

A 50 per cent. chemically pure grape sugar, dissolved in normal saline, was slowly introduced into the jugular vein. 10 grams of sugar to every kilo. of the dog's weight were the most usual quantities employed, and the whole introduced in about an hour.

After the necessary treatment of the various organs, the quantity of sugar was estimated by Allihn's method, the quantity of lactic acid by Drechsel's method, and the quantity of glycogen by Kulz's method. Alcohol, acetone, acetoacetic acid, $\beta$-oxybutyric acid, and ammonia were tested for in the usual way.

The following is a summary of the facts obtained:—

1. *Nervous Phenomena.*—It was noticed that large quantities of sugar gave rise, in dogs, to a series of symptoms pointing to nerve centre poisoning, their severity varying in different cases.

These nerve symptoms were generally preceded by, or attended with efforts at vomiting. But, from their stomachs being empty, the animals only brought up frothy mucus.

In some cases, the irritation of the nerve centres was only shown by muscular movements, causing a trembling of the skin. In other instances the muscular contractions were sufficiently severe to cause a quivering of the limbs, or even well-marked convulsions.

During the convulsive stage the pupils were contracted, although still reacting to light. The respirations were greatly increased. Around the mouth frothy mucus collects. The convulsions alternated with periods of rest, which gradually prolonged themselves until the dog seemed to be asleep. The convulsions sometimes were followed by profound coma, out of which the animal could not be roused. In some of the dogs the coma set in without any preliminary convulsive stage. Both the convulsive and comatose state always passed off when the ureters were loosed, while in some instances all the symptoms disappeared of their own accord.

10 grams of sugar per kilo. usually proved fatal to small dogs during the convulsion stage, from the respirations suddenly ceasing. Large dogs (of 20, or more, kilos. weight), showed only very mild symptoms, even after as much as 12 grams of sugar per kilo. weight were employed.

From the order of appearance and disappearance of the symptoms above alluded to, it seemed as if the sugar, by the breaking up of its molecule, yielded a poison or poisons, which, on being further transformed, became harmless.

It is worthy of note that none of these symptoms occur when sugar is absorbed from the intestines, no doubt for the same reason as they do not occur when only small quantities of sugar are injected into a vein; namely, because the intermediate products are never present at any one time in sufficient quantity to produce them.

2. *The quantity of sugar that remained as sugar in the different tissues* of the body was estimated at various periods of time after the completion of its injection.

(*a.*) The *quantity of sugar in the blood* at different periods of time after its injection into the jugular vein, the ureters being ligatured.

| No. of experiment. | Time after completion of sugar injection. | Sugar in 100 parts of blood. |
|---|---|---|
| IX | Before injection | ? |
| | 1 hour after | ? |
| | 6 hours after | 0·095 |
| X | Before injection | 0·112 |
| | 1 hour after | 0·438 |
| | 3 hours after | 0·126 |
| | 6 hours after | 0·084 |
| XI | Before injection | 0·079 |
| | Immediately after | 0·676 |
| | 4 hours after | 0·311 |
| | 6 hours after | 0·118 |

From this it was seen that the quantity of sugar goes on diminishing after its injection, and that by the sixth hour it had reached (Exp. X) even a lower point than what it stood at after the twenty-four hours' fast.

(*b.*) *The quantity of sugar found in the liver*, as compared with that met with in the blood.

| No. of experiment. | Time after completion of sugar injection. | Sugar in 100 parts of | |
|---|---|---|---|
| | | Moist liver. | Blood. |
| IV | 6 h. 20 m. | 0·92 | 0·056 |
| III | 7 h. | 1·72 | 0·025 |

The great difference observable between the quantity of sugar in the liver and in the blood shows how imperfect must be the passage from the liver into the general circulation of such a diffusible substance as sugar. This is all the more remarkable when we remember that the liver cells are surrounded not only by blood, but also by lymph, vessels.

(*c.*) *The Presence of Sugar in the matter vomited.*—As previously mentioned, several of the dogs vomited a quantity of mucus after the injection of the sugar.

In the cases in which the vomit was analysed it was found to contain sugar in small quantities.

(*d.*) *Quantity of Sugar in the Alimentary Tract.*—In order to ascertain if any of the sugar was eliminated into the alimentary tract, the contents of the stomach and intestines of three dogs were analysed. As all were in a fasting condition, contamination from food had not to be feared.

In only one case was sugar found in the stomach, and then only to the amount of 0·174 gramme. In no case was it found in the intestines. So it had, in all probability, been eliminated by the salivary glands and swallowed with the saliva. I am led to this opinion on account of Weyert having pointed out that when large quantities of sugar are injected into a vein, it is, in small quantities, eliminated with the saliva.

One may therefore, I think, consider that the alimentary tract does not eliminate sugar.

(*e.*) *Quantity of sugar in the œdematous exudations*, collected from the kidneys and upper part of ureters after their ligature.

| No. of experiment. | Time after completion of sugar injection. | Quantity of fluid. | Quantity of sugar. | Sugar in 100 parts of | |
|---|---|---|---|---|---|
| | | | | Œdematous fluid. | Blood. |
| | | c.c. | | | |
| V | 1 h. 45 m. | 16 | 0·463 | 2·89 | 0·290 |
| II | 7 h. | 4 | 0·104 | 2·60 | 0·064 |
| I | 7 h. | 10 | 0·196 | 1·964 | — |
| III | 7 h. | 11 | 0·105 | 0·96 | 0·025 |

Here it is seen that the quantity of sugar in the œdematous fluid, as was observed in the case of the liver, is greater than in the blood.

(*f.*) *Quantity of Sugar in the Urine.*—In order to ascertain if sugar passed out in the urine six or more hours after its injection, the ligatures were removed from the ureters in five of the cases and the urine passed during the following night collected. In one case only was there as much as 0·06 per cent. of sugar found in the urine. Consequently one may conclude that after sugar is injected and the ureters kept ligatured six or more hours, no sugar is eliminated in the form of sugar by the kidneys. The small quantity found in the one case could have been derived from the exudation which had accumulated in the kidneys and ureters during the time of ligature.

3. *Quantity of glycogen found in the liver and muscles* after the injection of sugar into the jugular vein.

| No. of experiment. | Time after completion of sugar injection. | Glycogen in 100 parts of | |
|---|---|---|---|
| | | Liver. | Muscle. |
| V | 1 h. 45 m. | 0·43 | 0·22 |
| IV | 6 h. 20 m. | 0·52 | 0·39 |
| I | 7 h. | 2·31 | 0·81 |
| II | 7 h. | 1·75 | 0·09 |
| III | 7 h. | 9·65 | — |

The results obtained from these five experiments show that the quantity of glycogen met with after the injection of 10 grammes of sugar per kilo. of dog's weight is well within the ordinary limits. Consequently one cannot say that any very appreciable amount of glycogen had been formed from the sugar that had been artificially introduced into the general circulation.

4. As it was thought possible that *lactic acid* might be one of the substances into which sugar split up in the organism, quantitative estimations were made of it in the blood and certain of the tissues.

(*a.*) *Quantity of lactic acid in the blood* at various times after the intravenous injection of sugar.

| No. of experiment. | Time after completion of sugar injection. | Lactic acid in 100 parts of blood. |
|---|---|---|
| IX | Before injection | 0·106 |
| | 1 hour after | 0·112 |
| | 6 hours after | 0·069 |
| X | Before injection | 0·071 |
| | 1 hour after | 0·107 |
| | 3 hours after | 0·104 |
| | 6 hours after | 0·084 |
| XI | Before injection | 0·097 |
| | Immediately after | 0·134 |
| | 4 hours after | 0·116 |
| | 6 hours after | 0·110 |

It is here seen that a marked increase of the lactic acid takes place after the injection of sugar. Further, that after the fourth hour it decreases slower than does the percentage of sugar itself in the blood. In the following table the effects of this slower decrease is well shown.

| No. of experiment.. | XV. | XVI. | IV. | III. | VI. |
|---|---|---|---|---|---|
| Time after injection | 4 hours. | 5 hours. | 6 hours. | 7 hours. | 25 hours. |
| Sugar per cent. .... | 0·072 | 0·073 | 0·056 | 0·025 | 0·090 |
| Lactic acid per cent. | 0·087 | 0·082 | 0·090 | 0·090 | 0·130 |

These results give an average of 0·065 per cent. of sugar as against 0·096 per cent. of lactic acid in the blood. Whereas, in dogs on normal diet, Gaglio has shown the quantity of sugar in the blood was more than the quantity of lactic acid.

(*b.*) *Quantity of lactic acid in the liver and muscles* as compared with the amount in the blood after ligature of the ureters and the injection of 10 grammes of sugar per kilo. of dog's weight.

| No. of experiment. | Time after completion of sugar injection. | Lactic acid in 100 parts of | | |
|---|---|---|---|---|
| | | Liver. | Muscle. | Blood. |
| V | 1 h. 45 m. | 0·339 | 0·171 | 0·135 |
| IV | 6 h. 20 m. | 0·135 | 0·112 | 0·090 |
| III | 7 h. | 0·031 | 0·011 | 0·090 |

The liver is thus seen to contain more lactic acid than the muscles, while, on the other hand, the blood sometimes contains more and sometimes less than both the liver and muscles.

From this it might be inferred that if the amount of a substance in any given part of the body yields a clue to the seat of its formation, it is probable that the liver is the principal seat of the lactic acid formation, as pointed out by Wyssokowitzsch.

(*c.*) *Quantity of lactic acid excreted in the urine*, the ureters having been ligatured for six or more hours after the injection of sugar into the jugular vein.

| No. of experiment. | Ureters having been ligatured. | Time during which the urine was collected. | Quantity of urine. | Contained lactic acid. | |
|---|---|---|---|---|---|
| | | | | Total quantity in grammes. | Per cent. |
| | | | c.c. | | |
| XV | 6 h. | First 12 hours | 475 | 0·115 | 0·024 |
| | | Following 24 hours | 600 | 0·062 | 0·010 |
| VIII | 6 h. | „ 12 „ | 230 | 0·173 | 0·075 |
| XI | 6 h. 40 m. | „ 24 „ | 650 | 0·571 | 0·088 |
| V | 9 h. | „ 12 „ | 162 | 0·562 | 0·346 |

From these results it appears that lactic acid is not only increased in the blood after the injection of sugar, but that it is at the same time excreted in the urine, whereas lactic acid is not known to occur in healthy dog's urine.

5. As *acetone, acetoacetic acid, and β-oxybutyric acid* are often found *in the urine* of diabetics, it was decided to examine it for these substances.

(*a.*) *Acetone and acetoacetic acid* were found to be present in all the five urines examined.

(*b.*) *β-Oxybutyric acid* was searched for in the urine both with the

polariscope and as α-crotonic acid, but could not, with any certainty, be demonstrated.

6. The *blood* was examined for *alcohol, acetone, and acetoacetic acid* by distilling it at a temperature of 102° C. by means of steam passed through it. The distillate being examined for alcohol and acetone. While in normal blood so treated neither alcohol nor acetone could be demonstrated, in the blood of dogs subjected to the sugar injection the presence of both of these substances was readily recognised.

Acetoacetic acid was searched for by acidifying the blood with sulphuric acid and then again distilling it. By this means its presence was also demonstrated in the blood of the sugared dogs.

7. As not only alcohol and acetone but likewise acetoacetic acid was found in the blood after the intravenous injection of sugar, it was decided to see how much *ammonia* could also be distilled off after adding magnesia to the blood. In the first place, as it was necessary to see if ligaturing the ureters caused an increase of the ammonia normally present in the blood. The blood of a dog in which the ureters alone had been ligatured was distilled, first immediately after and then a second time when the ureters had been ligatured five hours. The first blood yielded 0·025 per cent. and the second 0·024 per cent. of ammonia. So the ligaturing of the ureters had caused no increase in the quantity of ammonia present in the blood.

The same thing was then done with the blood from dogs before and after the intravenous injection of sugar.

| Weight of dog. | Ammonia obtained from 100 parts of blood. | |
|---|---|---|
| | Before the sugar injection. | 5 hours after. |
| kilos. | | |
| 29·5 | 0·025 | 0·034 |
| 27·5 | 0·018 | 0·017 |
| 5·0 | 0·042 | — |
| 3·8 | 0·039 | — |

It is thus seen the sugar injection had caused no increase in the quantity of ammonia in the blood.

It may be safely concluded that ammonia is not the cause of the nervous symptoms which followed the injection of 1 per cent. of sugar intravenously.

As these results again do not accord with those which follow on the injection of alcohol, we are led to suppose that they may be in some way or another connected with the presence in the blood of the abnormal substances, acetone and acetoacetic acid, which, as was seen, were not only found in the blood but likewise in the urine.

The possibility that the increase in the quantity of the lactic acid may likewise assist, if not be a material cause, in producing the nerve-symptoms, is also worthy of note.

That sugar, acting as sugar, was not their cause was shown by the symptoms not appearing until from a quarter to one hour after its injection. That is to say, not till the quantity of sugar present in the blood had already markedly decreased.

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# THE VALUE OF SUGAR AND THE EFFECT OF SMOKING ON MUSCULAR WORK.

By VAUGHAN HARLEY, M.D., M.R.C.P., *Teacher of Chemical Pathology, University College, London, and Grover Research Scholar.* (Two Figures in Text.)

(*From the Physiological Institute, Turin.*)

The metabolic changes occurring in the animal body although beset with many difficulties have of late years received much attention, and we are now slowly beginning to recognise and follow the chemical changes that take place in the continual breaking down and building up of new substances in the process of life.

The importance of carbohydrates in the production of muscular activity has been generally acknowledged by physiologists since the important experiments of Voit and Pettenkofer and Voit[1]. These observers showed that within certain limits both in dog and man muscular work was capable of taking place without the participation of the nitrogenous substances of the organism.

The chemical changes occurring during muscular activity have been investigated not only in the muscles after removal from the body but even when still in the animal, and undisturbed by operative interference. It has been shown by Ranke[2] and Du Bois Reymond[3] that a contracting muscle becomes acid, and that the acid formed is sarcolactic acid.

The experiments of O. Nasse[4], Brücke and S. Weiss[5] have shown that the glycogen which is diminished in the muscles during activity again accumulates in them during the periods of repose.

[1] Voit. *Ueber den Einfluss des Kochsalzes u. s. w. auf den Stoffwechsel.* München, 1860. Pettenkofer and Voit. *Zeit. f. Biol.* Vol. II. p. 459; 1866.

[2] T. Ranke. *Tetanus*, p. 329. Leipzig, 1865.

[3] Du Bois Reymond. *Arch. f. d. ges. Physiol.* Vol. XIII. p. 626.

[4] O. Nasse. *Ibid.* Vol. II. p. 97.

[5] Brücke and S. Weiss. *Wiener Acad. Sitzungsber.* Vol. LXIV. 1871.

The later researches of Chauveau and Kaufmann[1] have demonstrated that sugar disappears to a far greater extent from the blood supplying an active muscle than when at rest. This they showed by analysing the blood going to, and coming from, the masseter muscle of a horse during the act of chewing. They found that not only from 2·5 to 3 times more blood traversed the masseter during activity than while at rest, but that a thousand grams of muscle used 0·121 grams of sugar during repose, and 0·408 grams while chewing, i.e. four times more sugar is used up during activity. In these experiments the difference in the quantity of sugar in the analysed arterial and venous blood was not so great that it might not be partly due to the necessary errors. Seegen[2] showed that in a dog during struggling the venous blood contained less sugar than the arterial. In tetanising the muscles this result was reversed, which he considers might be due to the formation of some other reducing substance during the stimulation of the muscle. These facts seem to show that the carbohydrate (sugar) plays a very important rôle in the production of muscular energy.

Moreover the question as to whether or not muscular work can be produced by the proteids has still further lost its value, for it is now known that not only can carbohydrates be produced out of the proteids in the animal body, but even in the test tube.

The muscles not only increase in size by constant use but under the wear and tear of exercise the nitrogenous compounds are slowly destroyed, and the muscles therefore require proteids both for repair and formation of new substance.

The above chemical changes, known to take place during muscular activity, led me to believe that sugar when taken as food could be experimentally demonstrated to be an active generator of muscular energy. This fact never having been proved I decided to carry out the following research. Since sugar has become so cheap, it might be added in large quantities to the dietary of the working man, as a promoter of muscular power, and not merely be employed as it is at present as a mere condiment.

In order to render the results of the experiments conclusive it was necessary to find a means of estimating exactly the amount of work done by one particular set of muscles under a variety of conditions as regards diet, etc. For this being done it might not be unreasonably

[1] Chauveau and Kaufmann. *Comptes Rendus*, Vol. CIII. p. 1057; 1886; *Ibid.*, Vol. CIV. pp. 1126 and 1352; 1887.

[2] Seegen. *Central f. Physiol.* Vol. VII. p. 375; 1893.

supposed that the other muscles of the body would act in a like manner to those experimented upon. In a series of experiments made on myself I employed the ergograph (as invented by Professor Mosso[1]), by which means I was able to calculate the work done by the flexor muscles of the middle fingers.

I desire here to express my thanks to the kindness of Professor Mosso in placing his apparatus at my disposal. The experiments were carried out in September and October of 1892, in Turin; since then confirmatory results have been obtained by Ugolino Mosso.

While working the ergograph the finger used was made voluntarily to contract to its utmost limit, the weight being lifted each time as high as possible, all the force being put into each separate contraction. The contractions were made every two seconds. The weight used for the left middle finger always being 3 kilos, while for the right, as it was found to be able to lift a greater weight, 4 kilos were employed.

In order that the results might be as accurate as possible, the amount of work was calculated in kilogrammeters by two methods.

*Firstly.* The total amount of work up to the time of fatigue.

*Secondly.* The amount of work accomplished by thirty muscular contractions.

Throughout the series of experiments, except when specially mentioned to the contrary I daily partook of exactly the same diet, and as it had to be continued for a long time it was necessary to have it of a mixed character, so as to keep the health unimpaired.

The diet was as follows.

At 8 a.m., 2 rusks along with a cup of coffee and milk, without sugar.

At 12.30, soup, beef steak with vegetables and omelette with $\frac{1}{4}$ liter of red wine and a small cup of black coffee.

At 7 p.m., fried sole, roast beef and vegetables, quail and salad and a peach or pear, $\frac{1}{4}$ liter of red wine and small cup of black coffee. With the two latter meals, bread was taken and the quantities of each food were kept as nearly as possible the same.

When working the ergograph between each experiment a period of two hours was allowed to elapse. I found like Maggiora[2] that it required about two hours for the muscles to regain their working power after having been exhausted by fatigue. I further found, as he did, that

[1] The description of the instrument employed is given in *Arch. Ital. de Biologie*, Vol. XIII. p. 123; 1890—while a fuller paper is given *Arch. f. Anat. u. Physiol.* p. 89; 1890.

[2] Arnaldo Maggiora. *Arch. Ital. de Biologie*, Vol. XIII. p. 187; 1890.

if the fatigued arm was massaged for a few minutes the period of rest necessary to restore the working power of the fatigued finger was very markedly diminished.

It is of equal interest to notice that during the first few days of working with the ergograph I found that the will force did not attain immediately its full amount of power; the weight not being lifted to its maximum height by the first muscular contraction, in some cases, not even attaining its maximum until the third or fourth contraction. I noticed the curious fact that if I thought over it before attempting to make the contraction, the maximum was reached with the first contraction. The delay in obtaining the highest contraction was always more marked with the left than the right hand. This may be accounted for by my being right-handed. After my left hand became accustomed to using the ergograph I obtained the maximum power with the first contraction. It appears as if the will had to be trained to immediately yield its maximum nerve stimulus.

At first very irregular contractions were obtained instead of getting the gradual decline in force with each successive contraction as occurs in typical fatigue curves.

In my own case, as was the case with Lombard[1], even when the fatigue was so great that the will only responded in the shape of a feeble muscular contraction, the weight being only just moved, not raised, on continuing, so to speak to force the will, the weight was again raised a little, and each successive contraction raised it higher and higher for from 4 to 8 contractions, when it again began to diminish. In some cases this result could be obtained as many as five or more times. In these instances profuse sweating especially of the hands occurred. Sometimes the sweating was most marked on the hand and arm in use, but as a rule both sides were equally affected.

It is necessary to mention that in consequence of finding, as above stated, that there were such well marked successive alternative periods of exhaustion and restoration of the muscular power, the amount of work done was reckoned only up to the first onset of exhaustion.

### Diurnal variations in the quantity of work performed.

That the amount of work done by the same set of muscles at different times of the day varied, was shown by Lombard[2], and the

[1] Warren Lombard. *Arch. Ital. de Biol.* Vol. XIII. p. 371; 1890.
[2] Warren Lombard. This *Journal*, Vol. XIII. p. 1; 1892.

result of my experiments tends to confirm the fact of there being a diurnal rise and fall in the power of doing voluntary muscular work, in the same way as there is a diurnal rise and fall in bodily temperature, pulse, etc. In order to show this plainly I have put together in the following chart (Chart I.) the average amount of work done in the space of 12 hours during six days by the right middle finger in raising a weight of 4 kilograms and by the left a weight of 3 kilograms, the food being always taken at the same hours and the same kind of diet strictly adhered to on all three days[1].

TABLE SHOWING DIURNAL RISE AND FALL IN VOLUNTARY MUSCULAR POWER ON ORDINARY DIET.

| Time of day | Time before fatigue occurred. Seconds | Total work. Kilogrammeters | Work accomplished by 30 contractions. Kilogrammeters |
|---|---|---|---|
| 9 a.m. | 110 | 6·202 | 3·849 |
| 10 ,, | 118 | 6·428 | 3·952 |
| 11 ,, | 138 | 8·743 | 4·932 |
| 12 ,, | 118 | 6·993 | 4·277 |
| 1 p.m. | 144 | 9·520 | 5·643 |
| 2 ,, | 138 | 8·203 | 4·950 |
| 3 ,, | 156 | 9·895 | 5·313 |
| 4 ,, | 142 | 7·848 | 4·509 |
| 5 ,, | 152 | 8·882 | 4·992 |
| 6 ,, | 124 | 8·663 | 4·662 |
| 7 ,, | 122 | 7·206 | 4·589 |
| 8 ,, | 144 | 8·780 | 5·011 |

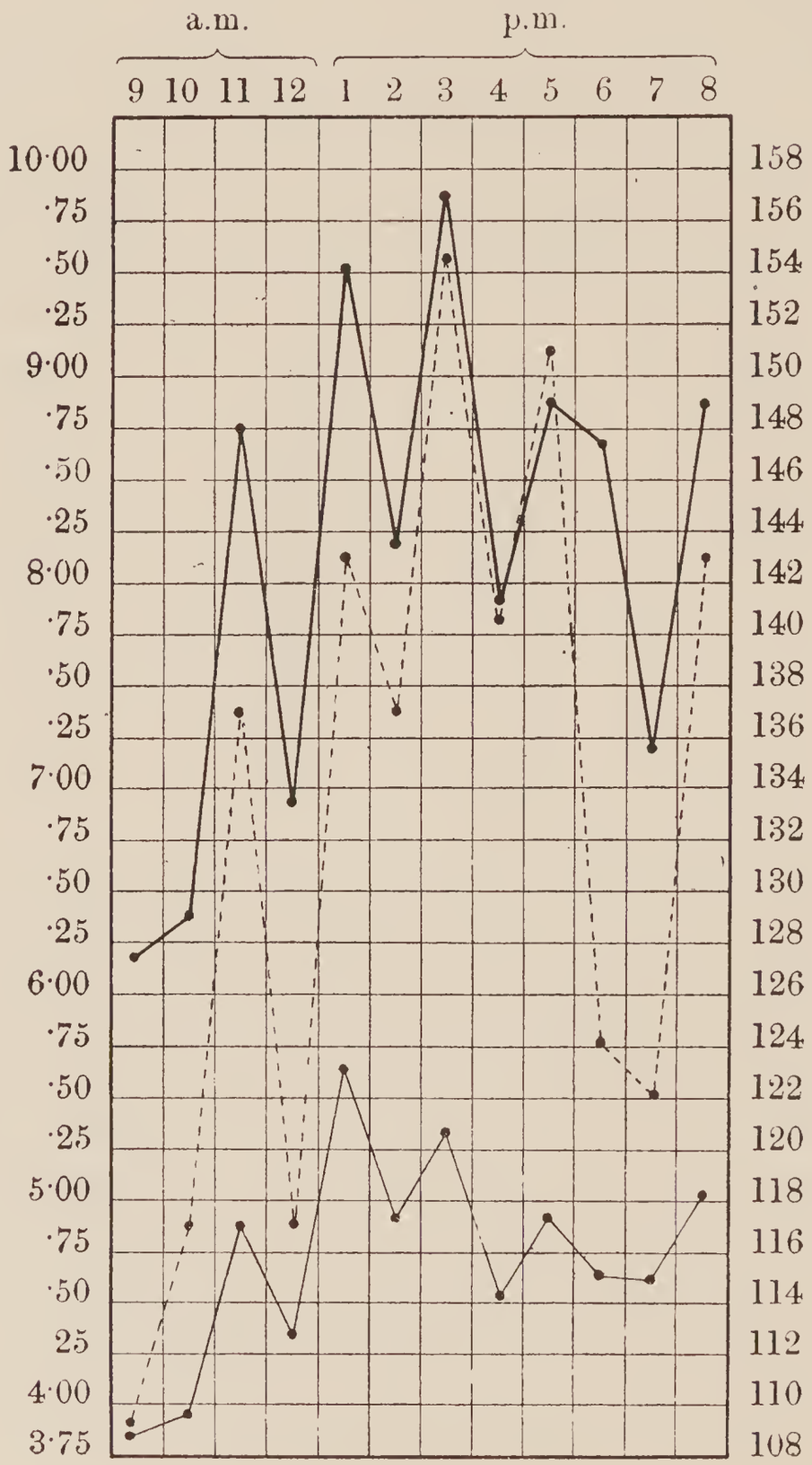
Instead of the greatest amount of work being done, as one would have expected, on rising in the morning after a good night's rest, it is here seen that at 9 a.m. the smallest amount of work was accomplished, and still further the power of doing muscular work increased each hour up to 11 a.m. Immediately after lunch there is a marked rise (1 p.m.) followed within the next hour (2 p.m.) by a fall; while an hour later, that is to say at 3 p.m., the amount of work accomplished reached the maximum, which for some unexplained cause was speedily followed by a notable fall at 4 p.m., again to be succeeded by a rise at 5 p.m., after which a progressive fall took place during each successive hour until dinner. That these alternative rises and falls in the muscular power cannot be accounted for by diet alone is rendered apparent by

[1] Dinner taken at 7.10 p.m.

the fact that the morning rise continued up to 11 a.m. though the breakfast was very light and taken at 8 a.m.

Chart I. Diurnal Variation in Voluntary Muscular Work. Ordinary diet. Average of 6 days.

The upper continuous line indicates—total work.
The broken ,, ,, —time before fatigue set in.
The lower continuous ,, ,, —work accomplished by 30 contractions.



Maggiora[1] showed that muscular exhaustion, caused by fasting, disappeared immediately on taking food and that it cannot be said to be due to a cerebral reflex action, as electric instead of voluntary stimuli showed the same effect. He consequently concludes that even a small absorption of food and its assimilation is sufficient to supply material to the muscles. The fact of the maximum amount of work being accomplished at 3 p.m.—$2\frac{1}{2}$ hours after lunch—might be due to the principal part of the nourishment having by this time been assimilated. But why there was a diminution in the muscular power at 2 and 4 p.m. I am at a loss to explain.

The fall at 5 to 7 again may be thought to be due, in part at least, to the want of nourishment; while the rise at 8 p.m. is readily accounted for by the restorative effects of dinner. In the chart (Chart I.) it is seen that the time before fatigue set in rose and fell with the total work done.

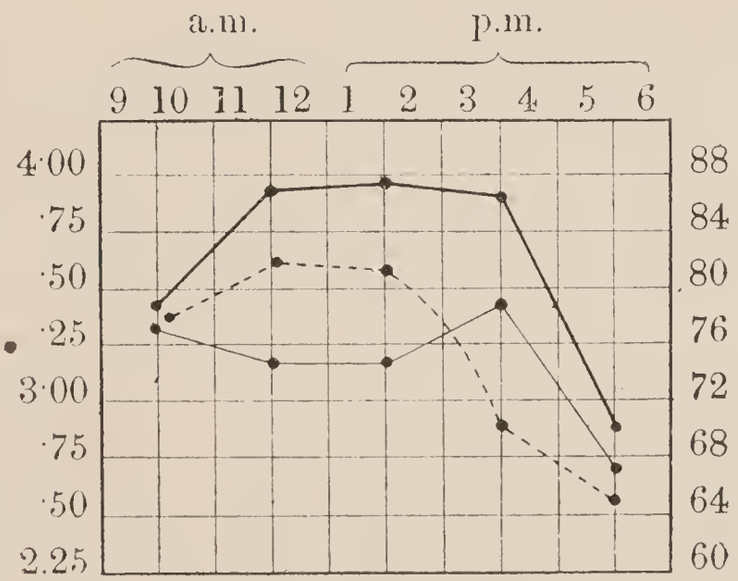
The work accomplished as calculated by 30 voluntary contractions, that is to say in 1 minute, exhibited a corresponding rise and fall.

The diurnal variations in the muscular power are points of much importance in drawing conclusions from the results of an investigation on the value of sugar in increasing voluntary muscular power, as it

CHART II. Diurnal Variation of Voluntary Muscular Work. Fasting Day.

Average of two hands.

The upper continuous line indicates—total work.
The broken " " —time before fatigue set in.
The lower continuous " " —work accomplished by 30 contractions.




[1] Maggiora. *Loc. cit.*

shows the absolute necessity of strictly comparing the amount of work done at precisely the same hours of the day if errors in its appreciation are to be avoided. The value of this remark is particularly noticeable by the marked increase in muscular power which occurs in the afternoon.

In the series of experiments made during a 24 hours' fast, it was still found that more work was done from 11.30 a.m. to 4.30 p.m. than at 9.30 a.m. The experiments were however scarcely sufficiently numerous to admit of definite conclusions being drawn from them.

TABLE SHOWING DIURNAL RISE AND FALL IN VOLUNTARY MUSCULAR POWER. Average of work done by right and left middle finger on day without food.

| Time of day | Time before fatigue occurred. Seconds | Total work. Kilogrammeters | Work accomplished by 30 contractions. Kilogrammeters |
|---|---|---|---|
| 9.30 a.m. | 78 | 3·408 | 3·372 |
| 11.30 „ | 82 | 3·922 | 3·193 |
| 1.30 „ | 81 | 3·997 | 3·203 |
| 3.30 „ | 69 | 3·947 | 3·488 |
| 5.30 „ | 66 | 2·881 | 2·743 |

Another point was to ascertain the effects of regular exercise, independently of food, on muscular energy, for it is well known that the exercise of a given set of muscles causes them to increase in size and at the same time renders them capable of performing more work. This physiological gain in muscular power was well marked in my experiments, as the same set of muscles were always exercised by the ergograph.

TABLES SHOWING THE INCREASE OF MUSCULAR POWER AFTER 42 DAYS OF REGULAR EXERCISE. The work accomplished by the left middle finger in raising a weight of 3 kilos. On full diet and no smoking.

| Time of day | Time during which weight lifted. Seconds | Total work done in kilogrammeters | Time during which weight lifted. Seconds | Total work done in kilogrammeters | Gain in force. Kilogrammeters |
|---|---|---|---|---|---|
| 9.30 a.m. | 108 | 5·691 | 140 | 7·904 | + 1·758 |
| 11.30 „ | 116 | 5·883 | 148 | 8·787 | + 1·913 |
| 1.30 p.m. | 100 | 5·538 | 134 | 8·049 | + 2·511 |
| 3.30 „ | 136 | 5·952 | 154 | 7·755 | + 1·803 |
| 5.30 „ | 104 | 5·808 | 112 | 6·795 | + 0·987 |
| Total | 564 | 28·872 | 634 | 37·844 | + 8·972 = 24 p.c. |

The total amount of work done during the day is seen to have increased from 28·872 to 37·844 kilogrammeters. That is, there was a total increase of 24 p.c. of muscular energy.

At the same time it shows that the period at which fatigue came on was retarded from 564 to 634 seconds. The work done by the right hand yielded practically the same results.

In consequence of this, two days were always chosen for comparison, in the following tables, with only a short interval between them. Further when it was desired to be very accurate a day's interval was given between each work day so that neither the element of fatigue nor the influence of diet might vitiate the results obtained.

## Influence of Sugar on Muscular Energy when taken by itself.

In order to get a definite answer to the question, is sugar actually a muscular food? I determined to ascertain the difference in the muscular energy on two consecutive days of fasting, nothing but water being

TABLE COMPARING THE EFFECT OF FASTING WITH SUGAR ALONE. Increase of muscular power during 30 voluntary contractions by taking 500 grams of sugar, 200 grams at 8.30 a.m., 100 each at 11 a.m., 2 p.m. and 5 p.m.

| | Fasting | | | 500 grams of sugar | |
|---|---|---|---|---|---|
| Time of day | Arm | Weight. Kilos | Kilogrammeters of work by 30 contractions | Kilogrammeters of work by 30 contractions | Gain in work. Kilogrammeters |
| 9.30 a.m. | Left | 3 | 3·372 | 4·452 | + 1·080 |
| 11.30 ,, | ,, | ,, | 3·273 | 4·812 | + 1·539 |
| 1.30 ,, | ,, | ,, | 3·513 | 4·524 | + 1·011 |
| 3.30 ,, | ,, | ,, | 3·735 | 3·798 | + 0·063 |
| 5.30 ,, | ,, | ,, | 3·186 | 3·873 | + 0·687 |
| Total | | | 17·079 | 21·459 | + 4·380 = 25·646 p.c. |
| 11.20 a.m. | Right | 4 | 3·112 | 3·552 | + 0·440 |
| 1.45 p.m. | ,, | ,, | 2·892 | 3·200 | + 0·308 |
| 3.40 ,, | ,, | ,, | 3·240 | 3·860 | + 0·620 |
| 5.45 ,, | ,, | ,, | 2·300 | 4·704 | + 2·404 |
| Total | | | 11·544 | 15·316 | + 3·772 = 32·675 p.c. |

taken on one of the days and nothing but water plus a certain quantity of sugar on the other. That the experiments should be as accurate as possible, on both days the fluid was taken hot; so that on the sugar day as much as possible could be taken in a small bulk of water.

Further no smoking was allowed on either day. The sugar thus introduced into an empty stomach would of course be quickly absorbed. Albertoni[1] showed that nearly 60 p.c. of the amount taken would be absorbed in the first hour, and that taking the sugar solution warm, contrary to what would be expected, slightly hindered the rate of its absorption.

From the above table it is seen that sugar is really a muscular food, for on the day it was taken there was an increase of 25·646 p.c. in the work done by the left middle finger while the right middle finger showed an increase of no less than 32·675 p.c.

The effect of sugar in retarding the approach of fatigue was next estimated.

TABLE SHOWING TOTAL INCREASE IN MUSCULAR POWER AND RETARDATION OF FATIGUE BY TAKING 500 GRAMS OF SUGAR. 200 grams being taken at 8.30 a.m. and 100 grams at 11 a.m., 2 p.m. and 5 p.m.

| | Fasting | | 500 grams of sugar | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds | Total work. Kilogram-meters | Gain in work. Kilogram-meters |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 9.30 a.m. | 78 | 3·408 | 94 | 5·949 | + 2·541 |
| 11.30 „ | 76 | 3·816 | 106 | 9·627 | + 5·811 |
| 1.30 p.m. | 84 | 4·614 | 92 | 5·979 | + 1·365 |
| 3.30 „ | 66 | 4·245 | 118 | 6·381 | + 2·136 |
| 5.30 „ | 70 | 3·342 | 118 | 6·375 | + 3·033 |
| Total | 374 | 19·425 | 528 | 34·311 | + 14·886 = 76 p.c. |
| Right middle finger raising a weight of 4 kilos. | | | | | |
| 11.20 a.m. | 88 | 4·028 | 100 | 4·080 | + 0·052 |
| 1.45 p.m. | 78 | 3·380 | 114 | 4·376 | + 0·996 |
| 3.40 „ | 72 | 3·648 | 132 | 6·680 | + 3·032 |
| 5.45 „ | 62 | 2·420 | 138 | 6·564 | + 4·144 |
| Total | 300 | 13·476 | 484 | 21·700 | + 8·224 = 61 p.c. |

[1] Albertoni. *Arch. Ital. de Biol.* Vol. XVIII. p. 266; 1892.

It is here seen that the onset of fatigue was retarded 154 seconds (from 374 seconds to 528 seconds) by the taking of 500 grams of sugar; while the total work done by the middle finger of the left hand is seen to rise from 19·425 to 34·311 kgm., giving an increase of 14·886 kgm. or 76 p.c. At the same time the approach of fatigue in the right hand was in like manner retarded 184 seconds (from 300 to 484 seconds). The total work of the right middle finger was increased from 13·476 to 21·700 kgm., being a gain of 8·224 kgm. or 61 p.c.

Thus 500 grams of sugar when taken alone increased the work of the left 76, and of the right finger 61 p.c. over that done when no food was taken, while it retarded the amount of fatigue more than 150 seconds in each case.

When one looks more carefully into the results obtained in the above two tables they seem clearly to point to certain chemical changes having taken place in the organism.

For example the organism having been long without food, the left hand showed in thirty voluntary contractions at 1.30 p.m. a gain of 1·011 kgm. (3·513 : 4·524 kgm.) on the sugar day (no sugar had been taken since 11 a.m.), fatigue in this case was retarded only 8 seconds and a total gain of 1·365 kgm. (4·614 : 5·979 kgm.) of work was obtained.

Sugar was now taken at 2 p.m. which would supply some nourishment and at 3.30 p.m. fatigue was retarded and there was a total increase of work. During 30 voluntary contractions the gain in working power was only 0·063 kgm. (3·735 : 3·798 kgm.); fatigue did not set in until 52 seconds later, and the total working gain was 2·136 kgm. (4·245 : 6·381 kgm.). Sugar being again taken at 5 p.m. one would expect even a more marked advantage over the fasting day. In 30 voluntary contractions at 5.30 p.m. there was a gain of 0·687 kgm. (3·186 : 3·873 kgm.) while fatigue was delayed 48 seconds and the total gain in work was 3·033 kgm. (3·342 : 6·375 kgm.).

This is explained by the carbohydrates present in the muscles being (during fasting) small in amount and derived in all probability principally from the proteids of the organism. In consequence the work done during the first 30 contractions is in both cases nearly equal, since enough carbohydrates are present to yield working material for this short time. When however these carbohydrates are used up, fresh must be supplied from the proteids and the supply does not keep pace with the demand; fatigue thereupon sets in and the amount of total work is diminished. On the sugar day, the sugar supplied the muscles

with a carbohydrate already formed into a suitable working material and fatigue is consequently retarded and the total work increased.

It became an interesting point to compare the amount of work done on a full ordinary diet with that of 500 grams of sugar alone as in these cases mental stimulus could hardly play a part.

TABLE COMPARING THE WORK DONE BY 30 VOLUNTARY CONTRACTIONS ON A DAY WITH 500 GRAMS OF SUGAR WITH THAT OF A FULL DIET.

| On 500 grams of sugar | | | | On full diet | |
|---|---|---|---|---|---|
| Time | Arm | Weight | Kilogrammeters by 30 contractions | Kilogrammeters by 30 contractions | Gain in work. Kilogrammeters |
| 9.30 a.m. | Left | 3 | 4·452 | 4·041 | − 0·411 |
| 11.30 „ | „ | „ | 4·812 | 4·005 | − 0·807 |
| 1.30 p.m. | „ | „ | 4·524 | 4·997 | + 0·473 |
| 3.30 „ | „ | „ | 3·798 | 4·146 | + 0·348 |
| 5.30 „ | „ | „ | 3·873 | 3·786 | − 0·087 |
| Total | | | 21·459 | 20·975 | − 0·484 = 2·308 p.c. |
| 11.40 a.m. | Right | 4 | 3·552 | 4·008 | + 0·456 |
| 1.40 p.m. | „ | „ | 3·200 | 4·322 | + 1·122 |
| 3.40 „ | „ | „ | 3·860 | 4·224 | + 0·364 |
| 5.40 „ | „ | „ | 4·704 | 3·912 | − 0·892 |
| Total | | | 15·316 | 16·466 | + 1·150 = 6·984 p.c. |

The work accomplished by the left hand on the sugar day is actually seen to be more than on the full diet one, there being a total of 21·459 kgm. as against 20·975 kgm., i.e. a gain of 0·484 kgm. or 2·308 p.c. It is further seen that this gain is due to more work having been obtained in the morning and again at 5.30 p.m.

The right hand however shows a plus on the sugar day, only at 5.40 p.m., the sugar day yielding a total of 15·316 kgm. as against 16·466 kgm. on the full diet, i.e. a gain of 1·150 kgm. or 6·984 p.c.

The next step was to compare the effect of the sugar in retarding the approach of fatigue with that of a full diet day.

TABLE COMPARING THE EFFECTS OF 500 GRAMS OF SUGAR WITH THAT OF A FULL ORDINARY DIET.

| On 500 grams of sugar | | | On full diet | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Secon ls | Total work. Kilogram-meters | Gain in work. Kilogram-meters |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 9.30 a.m. | 94 | 5·949 | 106 | 6·531 | + 0·582 |
| 11.30 „ | 106 | 9·627 | 102 | 6·477 | – 3·150 |
| 1.30 p.m. | 92 | 5·979 | 140 | 7·538 | + 1·559 |
| 3.30 „ | 118 | 6·381 | 132 | 7·041 | + 0·660 |
| 5.30 „ | 118 | 6·375 | 126 | 6·186 | – 0·189 |
| Total | 528 | 34·311 | 606 | 33·773 | – 0·538 |
| The right middle finger raising a weight of 4 kilos. | | | | | |
| 11.40 a.m. | 100 | 4·080 | 122 | 7·556 | + 3·476 |
| 1.40 p.m. | 114 | 4·376 | 136 | 7·742 | + 3·366 |
| 3.40 „ | 132 | 6·680 | 126 | 7·504 | + 0·824 |
| 5.40 „ | 138 | 6·564 | 120 | 6·328 | – 0·236 |
| Total | 484 | 21·700 | 504 | 29·130 | + 7·430 |

Here the results are seen to be most interesting. The left hand actually shows a gain in total work done in favour of the saccharine nutriment, there being a deficit of 0·538 kgm. on the day of full diet. The fatigue however came on earlier when sugar alone was taken.

The gain in muscular power was most noticeable at 11.30 a.m., which may be accounted for by the fact that a breakfast of coffee and rusks contains less actual nourishment than 300 grams of sugar. This is proved by the fact that the most work done on the full diet was after lunch, which gradually declined towards 5.30 p.m. On the sugar day, as well as the morning gain, the advantage was marked at 5.30 after 200 grams of sugar had been taken at 2 and 5 p.m. The general conclusion arrived at is that sugar is a powerful muscular food.

Having thus settled the point as to the practical value of sugar as a food, the next point was to ascertain what influence it would exert on muscular energy when given in addition to ordinary diet.

## Influence of sugar on muscular work when added to an ordinary diet.

TABLE SHOWING EFFECT OF 200 GRAMS OF SUGAR TAKEN AT 9 A.M. AFTER A BREAKFAST OF COFFEE, MILK AND 2 RUSKS. The work accomplished by 30 voluntary contractions.

| Coffee, milk and rusks | | | | + Sugar | |
|---|---|---|---|---|---|
| Time of day | Arm | Weight. Kilos | Kilogrammeters of work by 30 contractions | Kilogrammeters of work by 30 contractions | Gain in work. Kilogrammeters |
| 9.30 a.m. | Left | 3 | 3·717 | 4·131 | + 0·414 |
| 11.30 „ | „ | „ | 3·915 | 4·254 | + 0·339 |
| Total | | | 7·632 | 8·385 | + 0·753 = 8·980 p.c. |
| 9.40 a.m. | Right | 4 | 3·272 | 4·436 | + 1·164 |
| 11.40 „ | „ | „ | 4·308 | 5·208 | + 0·900 |
| Total | | | 7·580 | 9·644 | + 2·064 = 21·402 p.c. |

In the morning's work there is seen to be a gain in the amount of muscular power produced by the taking of 200 grams of sugar. This gain is most marked at 9.30 a.m. and 9.40 a.m., while the increased energy of the sugar is still shown even as late as 11.30 a.m. and 11.40 a.m.

The left hand has accomplished 8·385 kgm. on the addition of sugar as against 7·632 kgm. which yields a gain of 0·753 kgm , i.e. 8·900 p.c.

The right hand showed even a still greater gain on the sugar day, 9·644 kgm. as against 7·580 kgm. which is a total gain of no less than 2·064 kgm., i.e. 21·402 p.c.

Having thus found sugar caused a gain in the work accomplished after a simple breakfast it was next necessary to see whether it likewise increased the time before fatigue set in.

From the following table it is seen that both with the left and right hand there was an increase in the total work done when 200 grams of sugar were taken. The increase of work with the left finger amounted to 0·751 kgm., i.e. 6·162 p.c.

The increase of work with the right finger was 5·416 kgm., i.e.

39·059 p.c. The fatigue came on in the left finger at the same time; in the right finger 70 seconds later.

TABLE SHOWING EFFECTS OF 200 GRAMS OF SUGAR TAKEN AT 9 A.M. AFTER AT 8 A BREAKFAST OF COFFEE, MILK AND 2 RUSKS.

| | Coffee, milk and rusks | | + Sugar | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds | Total work. Kilogram-meters | Gain in work. Kilogram-meters |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 9.30 a.m. | 112 | 5·711 | 110 | 5·733 | + 0·022 |
| 11.30 „ | 122 | 6·477 | 124 | 7·206 | + 0·729 |
| Total | 234 | 12·188 | 234 | 12·939 | + 0·751 = 6·162 p.c. |
| Right middle finger raising a weight of 4 kilos. | | | | | |
| 9.40 a.m. | 100 | 6·312 | 112 | 7·108 | + 0·796 |
| 11.40 „ | 122 | 7·556 | 180 | 12·176 | + 4·620 |
| Total | 222 | 13·868 | 292 | 19·284 | + 5·416 = 39·059 p.c. |

In these two experiments it is well seen that the taking of sugar, although it caused an immediate increase in the total work, this increase was most marked 2½ hours later, so that it could not be accounted for on the theory of mere psychical stimulation. In fact throughout the whole series of experiments it was noticed that sugar always yielded the greatest amount of total work about 2 hours after it was taken—a fact in conformity with what is known regarding its absorption.

In the experiments in which the work accomplished was only calculated for the first 30 muscular contractions the gain in work was most marked at 9.30 a.m., only half-an-hour after sugar was taken. This might be due to the sugar, during the time the experiment was carried on, being gradually absorbed, it was at once conveyed to the muscles as such and used up. While on the other hand, when the sugar had been absorbed some little time (2½ hours) and converted into glycogen, by requiring to be reconverted into sugar it was slower in supplying the muscles with carbohydrate nutriment and thus the time before fatigue set in was increased and the power of doing work more marked after the

first 30 contractions. For it is seen that at 11.40 the right hand was not fatigued for 58 seconds later (180—122), and it actually accomplished 4·620 kgm. more work on the day in which the sugar was taken. Having thus ascertained the influence of sugar when taken in addition to a frugal meal, I next tried what effect it would have when taken in addition to an ordinary full luncheon.

TABLE COMPARING THE EFFECTS OF 250 GRAMS OF SUGAR TAKEN WITH A FULL LUNCHEON AT 12.30 ON THE WORK ACCOMPLISHED WITH 30 MUSCULAR CONTRACTIONS.

| Luncheon | | | | + Sugar | |
|---|---|---|---|---|---|
| Time of day | Arm | Weight. Kilos | Kilogrammeters of work by 30 contractions | Kilogrammeters of work by 30 contractions | Gain in work. Kilogrammeters |
| 2 p.m. | Left | 3 | 4·721 | 5·280 | + 0·559 |
| 4 ,, | ,, | ,, | 4·935 | 4·638 | − 0·297 |
| 6 ,, | ,, | ,, | 4·785 | 4·860 | + 0·075 |
| Total | | | 14·441 | 14·778 | + 0·337 = 2·28 p.c. |
| 2.15 p.m. | Right | 4 | 3·904 | 6·124 | + 0·220 |
| 4.15 ,, | ,, | ,, | 6·060 | 6·884 | + 0·824 |
| 6.15 ,, | ,, | ,, | 5·536 | 5·772 | + 0·236 |
| Total | | | 17·500 | 18·780 | + 1·280 = 6·82 p.c. |

Even the addition of sugar to a full luncheon has caused a gain, in the amount of work obtained by 30 muscular contractions, of 0·337 kgm., i.e. 2·281 p.c. with the left hand; while with the right 1·280 kgm., i.e. 6·816 p.c. in the space of the afternoon. Although this is not so marked as compared with a frugal meal, it is interesting to note, that in both cases the gain was most seen in the work done by the right hand. In the next place it was necessary to see what increase might be produced in the resistance against fatigue, when sugar was added to a full meal, and if it also caused the increase of work principally after the first 30 contractions which might be explained on the glycogen theory.

TABLE SHOWING THE INFLUENCE OF 250 GRAMS OF SUGAR TAKEN IN ADDITION TO AN ORDINARY FULL LUNCHEON AT 12.30.

| | Luncheon | | + 250 grams of sugar | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds | Total work. Kilogram-meters | Gain in work. Kilogram-meters |
| Left middle finger lifting a weight of 3 kilos. | | | | | |
| 2 p.m. | 140 | 7·902 | 140 | 9·168 | + 1·266 |
| 4 „ | 130 | 7·533 | 150 | 8·511 | + 0·978 |
| 6 „ | 112 | 6·795 | 142 | 8·241 | + 1·446 |
| Total | 382 | 22·230 | 432 | 25·920 | + 3·690 = 16·599 p.c. |
| Right middle finger lifting a weight of 4 kilos. | | | | | |
| 2.15 p.m. | 170 | 11·888 | 172 | 11·216 | − 0·672 |
| 4.15 „ | 163 | 11·188 | 220 | 13·648 | + 2·460 |
| 6.15 „ | 130 | 8·516 | 142 | 9·392 | + 0·876 |
| Total | 463 | 31·592 | 534 | 34·256 | + 2·664 = 8·433 p.c. |

It is here seen that the addition of 250 grams of sugar to a full meal caused an increase of 3·690 kgm., i.e. 16·599 p.c. in the work done by the left middle finger during the next 6 hours and that fatigue was delayed 50 seconds. The right middle finger likewise showed an increase of work, 2·664 kgm., i.e. 8·433 p.c. The time of fatigue setting in was retarded 71 seconds.

I will now show the influence of sugar taken at different hours of the day in addition to ordinary diet. The experiment being divided into 3 parts by 350 grams of sugar being taken in divided portions, 100 grams at 8 a.m. with breakfast, 100 grams at 12 a.m. before lunch and 50 grams at 3.50 p.m.

TABLE SHOWING EFFECT OF 250 GRAMS OF SUGAR, WHEN ADDED TO A FULL DIET DAY, ON THE WORK ACCOMPLISHED BY 30 MUSCULAR CONTRACTIONS.

| Full diet | | | | + Sugar | |
|---|---|---|---|---|---|
| Time of day | Arm | Weight. Kilos | Kilogrammeters of work by 30 contractions | Kilogrammeters of work by 30 contractions | Gain in work. Kilogrammeters |
| 9.30 a.m. | Left | 3 | 3·642 | 4·947 | + 1·305 |
| 11.30 „ | „ | „ | 4·203 | 4·854 | + 0·651 |
| 1.30 p.m. | „ | „ | 4·872 | 4·590 | − 0·282 |
| 3.30 „ | „ | „ | 4·302 | 4·338 | + 0·036 |
| 5.30 „ | „ | „ | 3·975 | 4·836 | + 0·861 |
| Total | | | 20·994 | 23·565 | + 2·571 = 10·906 p.c. |
| 9.40 a.m. | Right | 4 | 4·436 | 5·668 | + 1·232 |
| 11.40 „ | „ | „ | 3·560 | 5·852 | + 2·292 |
| 1.40 p.m. | „ | „ | 4·084 | 5·848 | + 1·764 |
| 3.40 „ | „ | „ | 4·072 | 5·008 | + 0·936 |
| 5.40 „ | „ | „ | 3·640 | 5·348 | + 1·908 |
| Total | | | 19·792 | 27·724 | + 7·932 = 28·610 p.c. |

In this case there is a well-marked gain in the capability of doing muscular work, caused by the addition of sugar to an ordinary diet, the left middle finger accomplishing 2·571 kgm. more work on the sugar day, being a gain of 10·906 p.c., the right, on the same day doing 7·932 kgm. more work, i.e. 28·610 p.c.; this great gain in the work of the right hand is in part due to the fact that on the day of the full diet it did less than is usual, for it actually did even less than the left. It is however as well to give it here as these two days were arranged for comparison, being early in the experiments and with only a short interval between them. It is further noticed that there is a marked gain in power at 5.30 p.m. and 5.40 p.m., caused by the 50 grams of sugar that were taken at 3.50 p.m.; thus causing a rise in muscular power above that obtained at 3.30 p.m. instead of the diurnal fall which normally occurs at this time.

TABLE SHOWING TOTAL GAIN IN A DAY'S MUSCULAR WORK BY THE ADDITION OF 250 GRAMS OF SUGAR TO THE ORDINARY DIET.

| Full diet alone | | | + 250 grams of sugar | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds | Total work. Kilogram-meters | Gain in work. Kilos |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 9.30 a.m. | 108 | 5·691 | 114 | 6·741 | + 1·050 |
| 11.30 ,, | 102 | 6·219 | 106 | 6·651 | + 0·432 |
| 1.30 p.m. | 112 | 7·131 | 102 | 7·742 | + 0·611 |
| 3.30 ,, | 138 | 5·073 | 126 | 6·966 | + 1·893 |
| 5.30 ,, | 84 | 4·830 | 108 | 7·221 | + 2·391 |
| Total | 544 | 28·944 | 556 | 35·321 | + 6·377 = 22·032 p.c. |
| Right middle finger lifting a weight of 4 kilos. | | | | | |
| 9.40 a.m. | 112 | 7·108 | 172 | 11·664 | + 4·556 |
| 11.40 ,, | 108 | 7·512 | 150 | 10·360 | + 2·848 |
| 1.40 p.m. | 146 | 8·420 | 148 | 10·392 | + 1·972 |
| 3.40 ,, | 126 | 7·236 | 148 | 8·880 | + 1·644 |
| 5.40 ,, | 104 | 7·752 | 158 | 10·368 | + 2·616 |
| Total | 596 | 38·028 | 776 | 51·664 | + 13·636 = 35·858 p.c. |

It will be noticed that in this case the left finger accomplished 28·944 kgm. on a full diet day, while by the addition of 250 grams of sugar to the same diet, it was enabled to do 35·321 kgm. The actual gain in work done by the sugar being 6·377 kgm., i.e. 22·032 p.c. The advantage in the retardation of fatigue was only 12 seconds. The right finger on the other hand under similar circumstances did with the sugar 51·664 kgm. as against 38·028 kgm. without it, the total gain in the muscular work being 13·636 kgm., i.e. 35·858 p.c. The advantage gained in the increase of time before fatigue set in was more marked, being no less than 180 seconds as against 12 seconds in the case of the left hand.

As these days were at the early part of the experiments before the muscles had been by continual use developed into doing the most work

with the least trouble, I will now give another set of examples carried out at the end of the series. This is all the more important as it would resemble the working man's condition who was doing continually muscular work.

The sugar in these cases was taken with meals, 150 grams being taken at breakfast and 100 grams at lunch; on both days 3 cigars were smoked.

TABLE COMPARING THE MUSCULAR WORK ACCOMPLISHED BY 30 CONTRACTIONS WITH ORDINARY DIET AND THAT OBTAINED ON THE ADDITION OF 250 GRAMS OF SUGAR.

| Full diet alone | | | | + Sugar | |
|---|---|---|---|---|---|
| Time of day | Arm | Weight. Kilos | Kilogrammeters of work by 30 contractions | Kilogrammeters of work by 30 contractions | Gain in work. Kilogrammeters |
| 10 a.m. | Left | 3 | 4·518 | 4·746 | + 0·228 |
| 12 — | ,, | ,, | 4·770 | 5·196 | + 0·426 |
| 3 p.m. | ,, | ,, | 4·698 | 5·280 | + 0·582 |
| 5 ,, | ,, | ,, | 4·566 | 4·638 | + 0·072 |
| 7 ,, | ,, | ,, | 4·665 | 4·860 | + 0·195 |
| Total | | | 23·217 | 24·720 | + 1·503 = 6·080 p.c. |
| 10.15 a.m. | Right | 4 | 5·380 | 5·628 | + 0·248 |
| 12.15 ,, | ,, | ,, | 6·140 | 5·704 | − 0·436 |
| 3.15 p.m. | ,, | ,, | 4·168 | 6·124 | + 1·956 |
| 5.15 ,, | ,, | ,, | 5·472 | 6·884 | + 1·412 |
| 7.15 ,, | ,, | ,, | 5·044 | 5·772 | + 0·728 |
| Total | | | 26·204 | 30·112 | + 3·908 = 12·978 p.c. |

We see here again there is an increase in the muscular work on the sugar day, the left hand doing 1·503 kgm., i.e. 6·080 p.c. more work, and the right 3·908 kgm., i.e. 12·978 p.c.

It is now necessary to see what the effect on fatigue the sugar had in this case.

TABLE SHOWING THE TOTAL GAIN IN MUSCULAR WORK AND FATIGUE CAUSED BY THE ADDITION OF SUGAR TO AN ORDINARY DIET.

| | Full Diet | | + Sugar | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds. | Total work. Kilogram-meters | Gain in work. Kilogrammeters |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 10 a.m. | 134 | 7·794 | 130 | 7·850 | + 0·056 |
| 12 — | 132 | 7·794 | 140 | 8·421 | + 0·627 |
| 3 p.m. | 114 | 6·558 | 140 | 9·168 | + 2·610 |
| 5 „ | 152 | 8·049 | 150 | 8·511 | + 0·462 |
| 7 „ | 132 | 7·755 | 142 | 8·241 | + 0·486 |
| Total | 664 | 37·950 | 702 | 42·191 | + 4·241 = 10·052 p.c. |
| Right middle finger raising a weight of 4 kilos. | | | | | |
| 10.15 a.m. | 152 | 9·856 | 182 | 11·188 | + 1·332 |
| 12.15 p.m. | 150 | 10·108 | 160 | 10·144 | + 0·036 |
| 3.15 „ | 154 | 8·996 | 172 | 11·216 | + 2·220 |
| 5.15 „ | 172 | 11·732 | 220 | 13·648 | + 1·916 |
| 7.15 „ | 150 | 9·732 | 142 | 9·392 | − 0·340 |
| Total | 778 | 50·424 | 876 | 55·588 | + 5·164 = 29·290 p.c. |

In these experiments is seen a prolongation in the time before fatigue set in caused by the sugar, the left hand being capable of working 38 seconds longer and the right 96 seconds on the sugar day.

The gain in total muscular work is also well marked, the left hand doing 4·241 kgm., i.e. 10·052 p.c. more work on the sugar day, while the right hand did 5·164 kgm. more, i.e. 9·290 p.c.

That the above results were not due to any mere voluntary effort on my part, that is to say, from trying to do more work, will be clear to any one accustomed to work with the ergograph, for as Lombard says one often does less work when one tries to do more under such circumstances. On many occasions I too observed that after finishing working and even seeing the tracing, I imagined I had done more work than was really found to be the case on calculating the results.

The results obtained from this series of experiments show that the addition of large quantities of sugar to an ordinary diet is of the greatest nutritive value, and I think they prove that sugar should no

longer be regarded as a mere condiment but looked upon as one of the most useful articles of food. By the reason of its cheapness it could with great advantage be added in much larger quantities than at present to any child's and working man's dietary.

During the experiments so far quoted no smoking (except when specially mentioned to the contrary) was permitted, as various writers, Lombard, &c. consider that it is detrimental to muscular work. I performed a few experiments to see what effect was produced in my own case with moderate smoking.

### Influence of Smoking on Muscular Energy.

TABLE COMPARING THE WORK DONE DURING TWO DAYS ON A FULL DIET, ON ONE OF WHICH FOUR CIGARS WERE SMOKED, ON THE OTHER NONE[1].

| | Diet alone | | + Four cigars | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds | Total work. Kilogram-meters | Gain or otherwise. Kilogrammeters |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 9.30 a.m. | 140 | 7·902 | 104 | 7·449 | + 0·453 |
| 11.30 „ | 148 | 8·787 | 130 | 7·533 | + 1·254 |
| 1.30 p.m. | 134 | 8·049 | 140 | 7·902 | + 0·147 |
| 3.30 „ | 154 | 7·755 | 130 | 7·533 | + 0·222 |
| 5.30 „ | 112 | 6·595 | 112 | 6·795 | − 0·200 |
| Total | 688 | 39·088 | 616 | 37·212 | + 1·876 = 5·041 p.c. |
| Right middle finger raising a weight of 4 kilos. | | | | | |
| 9.45 a.m. | 122 | 8·928 | 152 | 9·884 | − 0·956 |
| 11.45 „ | 140 | 10·860 | 150 | 10·508 | + 0·352 |
| 1.45 p.m. | 172 | 11·732 | 170 | 11·888 | − 0·156 |
| 3.45 „ | 154 | 9·732 | 163 | 11·188 | − 1·456 |
| 5.45 „ | 150 | 8·996 | 130 | 8·516 | + 0·480 |
| Total | 738 | 50·248 | 765 | 51·984 | − 1·736 = 3·339 p.c. |

In the above table it is seen that the left middle finger accomplished 1·876 kgm. more work, i.e. 5·041 p.c. on the day on which no smoking was done than on the day in which four cigars were smoked. However the right middle finger had a deficit of 1·736 kgm., i.e. 3·339 p.c. on the non-smoking day.

[1] Cigars at 9 a.m., 1 p.m., 3 p.m. and 4 p.m.

COMPARISON OF TWO MORNINGS' WORK ON THE ONE OF WHICH TWO CIGARS WERE SMOKED AT 9 AND 11 A.M.

| | No smoking | | Smoking | | |
|---|---|---|---|---|---|
| Time of day | Time during which lifted. Seconds | Total work. Kilogram-meters | Time during which lifted. Seconds | Total work. Kilogram-meters | Gain in work. Kilogrammeters |
| Left middle finger raising a weight of 3 kilos. | | | | | |
| 10 a.m. | 156 | 8·825 | 104 | 7·449 | +1·376 |
| 12 — | 132 | 8·421 | 158 | 8·787 | −0·366 |
| Total | 288 | 17·246 | 262 | 16·236 | +1·010 |
| Right middle finger raising a weight of 4 kilos. | | | | | |
| 10.15 a.m. | 122 | 9·884 | 152 | 8·928 | +0·956 |
| 12.15 p.m. | 140 | 10·860 | 150 | 10·021 | +0·839 |
| Total | 262 | 20·744 | 302 | 18·949 | +1·795 |

On these two mornings both the right and left fingers accomplished more work on the day when nothing was smoked.

The difference in effect before and after smoking a cigar, when a rest of two hours was allowed between the two experiments, was in no case so marked as in Lombard's experiments even when the cigar was only removed from the mouth immediately before commencing to work with the ergograph.

DIFFERENCE BEFORE AND AFTER SMOKING.

Left middle finger raising a weight of 3 kilos.

| | Time of day | Time during which lifted. Seconds | Total work. Kilogrammeters | Work done in 30 contractions. Kilogrammeters |
|---|---|---|---|---|
| | Cigar smoked from 3 to 3.30 p.m. | | | |
| a. | 1.30 p.m. | 140 | 7·538 | 4·997 |
| | 3.30 „ | 132 | 7·041 | 4·146 |
| | Cigar smoked from 11 a.m. until 12 noon. | | | |
| b. | 10 a.m. | 130 | 7·650 | 4·746 |
| | 12 — | 140 | 8·421 | 5·196 |
| | Again a cigar from 4.30 to 5 p.m. | | | |
| c. | 5 p.m. | 150 | 8·511 | 4·638 |
| | 7 „ | 142 | 8·241 | 4·860 |

In (a) a cigar was smoked up to the very moment the ergograph was commenced being worked.

The work done at 3.30 p.m. immediately after having smoked a cigar is less by 0·497 kgm. than that at 1.30 p.m. As a rule during these hours the amount of work accomplished is much about the same. One may therefore conclude that the cigar had somewhat of a detrimental effect. Fatigue was also hastened 8 seconds.

In (b) after having estimated the amount of work at 10 a.m. a cigar was slowly smoked from 11 to 12 when a plus of 1·771 kgm. was obtained. The time before fatigue came on was also prolonged 10 seconds. It has already been shown in an early part of this paper that during these hours the morning rise occurs which has not been obliterated by the cigar.

In (c) it was decided to try the effects of a cigar in another manner. As already shown in the afternoons from 5 to 7 p.m. there is invariably a falling off both in the amount of work accomplished and the time before fatigue set in. I therefore tried to see if, by smoking a cigar from 4.30 to the very minute the ergograph was first worked at 5 p.m., I could so diminish the work accomplished that less might be obtained than 2 hours later. At 5 p.m. 8·511 kgm. of work was done and at 7 p.m. only 8·241 kgm., giving a fall of 0·270. During the same hours fatigue set in 8 seconds earlier. In this case the cigar had again failed to hinder a diurnal variation.

It is needless to give more experiments as they all give unsatisfactory results.

It appears that moderate smoking in one accustomed to it neither increases the amount of work nor retards the approach of fatigue. On the contrary it perhaps slightly diminishes muscular power and hastens the onset of fatigue, though this could not be conclusively demonstrated on account of its neither hindering the diurnal increase nor stopping the diurnal decrease of muscular energy.

Before concluding I give an example of sugar counteracting the diurnal diminution in muscular power and acceleration of fatigue and likewise any diminution of these that might be caused by smoking a cigar.

In this experiment 5 minutes after finishing the work at 5.30 p.m. I took 100 grams of sugar and 10 minutes later lit a cigar and smoked continuously $1\frac{1}{2}$ cigars from 5.45 until the minute work was begun at 6.40 p.m. It is seen that the sugar caused an increase of 0·768 kgm. in the total work in spite of smoking, and that too at the

very time where there invariably is a diurnal fall of muscular energy. The fatigue too set in 12 seconds later.

TABLE SHOWING THE POWER OF SUGAR TO OBLITERATE THE DIURNAL DIMINUTION OF MUSCULAR ENERGY OCCURRING IN THE EVENING. 100 grams of sugar being taken at 5.35 p.m. and cigars smoked continually from 5.45 to 6.40 p.m.

Left middle finger raising a weight of 3 kilos.

| Time of day | Time during which lifted. Seconds | Total work. Kilogrammeters | Work done in 30 contractions. Kilogrammeters |
|---|---|---|---|
| 5.30 p.m. | 108 | 7·221 | 4·836 |
| 6.40 „ | 120 | 7·989 | 4·794 |

It is interesting to note that during the days I took sugar (even as much as 500 grams) I never in one single instance found any sugar in my urine, although frequently analysed during the day.

I obtained the same results when taking, during several days, 400 grams (13 oz.) daily of sugar, even upsetting my digestion so far as getting dyspepsia while working in the Sorbonne at Paris.

This agrees with the experiment of Kraus and Ludwig[1] who never found sugar in the urine after taking sugar. The cases in which Worm Müller[2] and Moritz[3] found notable quantities of sugar must I think be explained by the supposition that the persons experimented upon, though healthy, had a tendency to glycosuria. In the cases in which dogs were employed the reduction was in all probability due to some other reducing substance.

In my analysis not only did I employ Fehling's solution but never considered sugar present unless it gave, as well as a reduction, the phloridzine reaction. While working in Paris the fermentation test gave equally negative results.

## Conclusions.

1. The periods of digestion as well as the kinds of food taken have a marked influence on voluntary muscular energy.

2. Irrespective of the influence of food there is a periodical diurnal rise and fall in the power of performing muscular work.

[1] Kraus and Ludwig. *Wiener Med. Wochenschrift*, 1891, No. 46 and 48.
[2] Worm Müller. *Pflüger's Arch.* Vol. xxxiv. p. 576; 1884.
[3] Moritz. *Münchener Med. Woch.* 1891, p. 5.

3. More work can be done after than before midday.

4. The minimum amount of muscular power is in the morning about 9 a.m. The maximum about 3 in the afternoon.

5. Regular muscular exercise not only increases the size and power of the muscles but has the effect of markedly delaying the approach of fatigue.

6. The amount of work performed on a diet of sugar alone is almost equal to that obtained on a full diet; fatigue however setting in sooner.

7. In fasting large quantities of sugar (500 grams) can increase the power of doing muscular work during 30 voluntary contractions from 26 to 33 p.c.

While the total gain in a day's work may be 61 to 76 p.c., the time before fatigue sets in being also lengthened.

8. The effect of sugar is so great that when added to a small meal it can increase the muscular power during 30 contractions from 9 to 21 p.c., while the total increase in work may be from 6 to 39 p.c. and the approach of fatigue being at the same time retarded.

9. When added to a large mixed meal sugar can increase the muscular power of 30 contractions 2 to 7 p.c. The increase in total work being 8 to 16 p.c. and a marked increase in the resistance to fatigue is shown.

10. 250 grams of sugar taken in addition to a full diet increases the day's work. The work accomplished during 30 voluntary muscular contractions shows a gain of from 6 to 28 p.c., the total day's work giving an increase of power 9 to 36 p.c. and the time before fatigue sets in being lengthened.

11. Moderate smoking although it may have a slight influence in diminishing the power of doing voluntary muscular work, neither stops the morning rise nor when done early in the evening hinders the evening fall.

12. Sugar taken early in the evening is capable of obliterating the diurnal fall in muscular power that occurs at this time, and increases the resistance to fatigue.

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# "The Action of Gravity upon *Bacterium Zopfii*."

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(From the Pathological Laboratory of University College, London.)

[PLATES 1 AND 2.]

In May, 1892, Mr. Walter Spencer handed over to us the body of a cat in which he had discovered a double otitis media. Some of the pus was immediately inoculated upon gelatine, and two days later it was seen that the gelatine along the streak had liquefied, whilst the rest of the surface of the non-liquefied gelatine was covered by a

* Of the numerous photographs illustrating this paper, only five of the more typical ones are reproduced, namely, figs. 10, 12, 14, 23, 28. It has been thought better, however, to preserve the original numeration in the text, as the original photographs can be consulted if necessary.

regular growth of delicate white filaments. Re-inoculation proved the presence of more than one micro-organism, but we soon succeeded in isolating one which did not liquefy the gelatine, and which presented the exceedingly characteristic feather-like appearance well known to belong to *Bacterium Zopfii*. We were especially struck by the beautiful regular upward growth of the filaments upon the gelatine surface, for whether we placed the tubes with their mouth pointing upwards or downwards there appeared the same definite growth, provided the tubes were kept in a nearly vertical position. We accordingly immediately commenced an investigation, which we hoped might throw some light upon the meaning of this very definite symmetrical growth. With this end in view we first investigated the action of light, but whether we grew the bacterium in the light or in the dark, the symmetry remained the same. We now began to observe, however, that tubes which, after inoculation, were kept in a horizontal position exhibited an *irregular* growth. It therefore occurred to us to test the action of *gravity*, and we found in effect that revolving inoculated test-tubes slowly upon the clinostat* produced irregular growths, whilst *centrifugal force* induced, like gravity, a regular growth. *Bacterium Zopfii* was therefore negatively geotropic. These phenomena, viewed in the light of the more recent experiments upon the chemotactic and physiotactic properties of protoplasm—properties which appear already to throw very considerable light upon certain pathological problems—have led us to venture to record in detail our observations.

*Bacterium Zopfii* was accidentally discovered by Kurth† in the alimentary tract of the hen in 1883, and his description of the micro-organism, furnished from Zopf's laboratory, remains the standard one. In 1885 Professor Crookshank‡ obtained from the air in Johne's laboratory an organism which he named *Bacillus figurans* on account of its characteristically figured growth upon gelatine and agar; it proved to be identical with Kurth's bacillus. Lastly, as previously mentioned, we obtained our growth from the middle ear of the cat. These observations make it very probable that *Bacterium Zopfii* has a wide distribution, but whether it is pathogenic or not is still uncertain. We will, however, return to this point later on.

*Bacterium Zopfii* is pleomorphic; it is a slender organism of about the same diameter as *Bacillus anthracis*, and its segments are of very variable length. It occurs in the dissociated motile state, the elements being actively movable coccal, bacteroid, bacillary, and

* We desire to express our thanks to Professor Oliver for not only the use of this and other instruments, but also for his friendly criticism and advice during the research.

† 'Bot. Zeitung,' 1883.

‡ 'Lancet,' 1885.

twisted forms; the degree of spirillation in the latter motile forms, however, appears only very slight, and we have not, as yet, encountered the pronounced spirilla seen in *Cladothrix*. It occurs in non-motile filaments of great length, which may be unsegmented or segmented. A very striking feature of these filaments is their proneness to twist, to weave themselves into striking patterns, and to form aggregating zoögleaform masses, of equally curious shapes. The segments of the filaments may occur in the form of cocci, bacteria, bacilli, vibrios, spirilla, and spirochætæ and in the various double forms of these. Kurth grew the organism in broth and on gelatine, and obtained in the former the motile and long filamentous forms, whilst the twisted varieties appeared wanting: this we likewise have noted. In gelatine he found that it caused an imperceptible amount of liquefaction and grew out in a radiate manner, and formed characteristic spirals. Crookshank grew it upon agar, and obtained a feather-like growth which he figures; this, however, we have always failed to obtain upon that medium. Kurth drew attention to the sensitiveness of the organism to changes in temperature, to the hindering action of the air, and to the great necessity for plenty of oxygen.

### *The Growth of* Bacterium Zopfii *upon Gelatine.*

For our experiments we have always employed the 10 per cent. gelatine possessing a neutral or faintly alkaline reaction, but we have found no appreciable difference whether the organism was grown on gelatine with faintly alkaline or acidic reactions. We use the ordinary culture-tubes, Petri boxes, and a method of plate glass culture which we have found exceptionally useful. This method consists in placing a small piece of moist cotton wool in the bottom of a test-tube large enough to hold the ordinary $1 \times 3$ inch micro-slide; the test-tube is plugged, and the whole sterilised in the steam steriliser at 120° for 20 minutes. When cooled, a thin uniform layer of sterilised gelatine is very readily spread over the surface of the slide in the test-tube, which remains horizontal, by means of the balloon pipette of Pasteur: there is no fear of contamination. The test-tube is plugged and capped to prevent drying, and the slide is then always ready for inoculation. When a streak culture has been made upon the gelatine surface, and it is desired to examine the growth, the slide is removed and placed in slightly diluted spirit for a few hours, to fix the growth and extract the salts. The slide is then carefully dried, stained for a few seconds in gentian violet, washed with Gram's iodine, and nearly decolorised in spirit, again dried, mounted in Canada balsam, and covered with a sufficiently long cover-slip. By this method there is the least possible disturbance of the growth, and all our micro-

photographs have been taken from plates so prepared. The organism can always, however, be readily examined upon these gelatine slides without fixing or staining. The method of cover-slip impressions we have found not applicable in our case, as the growth is firmly embedded in the gelatine; it is useful, however, in the case of agar. For reasons which will be given later, it is necessary to observe under the microscope the ordinary test-tube growths *in situ* in the gelatine. For this purpose we rapidly warm the test-tube to just produce liquefaction of the surface of the gelatine in contact with the glass, and then slide it out upon a glass plate; a cover-slip is placed over the surface of the growth, and it can then be examined. Another method which we have employed, and one again which does not lead to any disturbance of the growth, is the well known method of drop cultures, but employing gelatine instead of a fluid medium.

Fig. 1 is a photograph of a 36 hours' growth upon gelatine, the result of a streak inoculation (see also fig. 12). The tube was kept vertical. It is the characteristic growth, *i.e.*, lines passing outwards and upwards at an angle of about 45°: the appearance is typically pinnate. In connexion with these vertical streak cultures we have noticed this very curious phenomenon, that no matter how crooked our original streak may be, yet the growth seems to form a new perfectly median axis for itself, from which the rami start; further, if instead of a vertical streak we make three or four streaks upon the surface of the gelatine at right angles to the long axis of the test-tube, the growth still tends to form a median line. These facts, coupled with our microscopic observations, pointed out to us that we might possibly be dealing with a branching phase similar to that met with in *Cladothrix dichotoma;* and, indeed, if we refer to Zopf's* drawings of *Cladothrix* we do recognize a pinnate arrangement of the so-called false branches of the filamentous organism. Billet† has termed this branched state the "filamentous," meaning thereby the "état d'accroissement proprement dit de la plante;" he has described it in *Cladothrix*, *Bacterium parasiticum*, *B. laminariæ*, *B. ureæ*, *B. Balbiani*, and *B. osteophilum*. In *Bacterium Zopfii* we shall regard the branching growths as corresponding to the "filamentous phase."

We soon found that we did not always obtain the characteristic growth, even in the test-tube; not only had the degree of sloping, as mentioned in the commencement, a considerable effect upon its regularity, but the temperature also exercises a marked effect. We obtained the best growths in a temperature of about 21° C. kept constant. In this way a perfect growth might be obtained in 24 hours, whilst if that portion of the test-tube which corresponded

* Schenk's 'Handbuch der Botanik.'

† 'Contrib. à l'Étude de la Morphologie et du Développement des Bactériacées.' Paris, 1890.

to the back of the gelatine was painted black, growth was still faster and might cover the surface in 12 hours. On the other hand we found accidentally that a reflecting surface retarded the growth. These latter phenomena we attributed to differences of radiation.

When next we directed our attention to the gelatine cultures on glass plates and in Petri boxes, we encountered a still greater number of irregularities. Upon the glass slides covered with a thin layer of gelatine we never obtained a good negatively geotropic growth; the usual condition was the irregularly branched appearance seen in figs. 15 and 16 under a low power. For the reasons of this we are still at a loss, unless it be the increased resistance of the gelatine. In the Petri boxes with a thickness of gelatine varying from $\frac{1}{4}$ to 1 inch, or even more, we obtained some instructive results. We never succeeded in getting symmetrical pinnate growths *on the surface* comparable to those in test-tubes; but that we obtained evidence of geotropism is manifest from the photographs, figs. 2, 3, 4, 5. In figs. 2 and 4 vertical streaks had been made; in fig. 3, a circular streak; and in fig. 5, a cross. The time occupied in the formation of these growths was relatively very much longer than in the case of test-tubes; moreover the filaments upon the surface rarely possessed the delicate character of that obtained in test-tube cultures; they had, in fact, as we shall subsequently see, the character of zoögleaform threads. In fig. 6 a horizontal streak has been made, and although the glass dish was kept vertical, an irregular growth has extended for an equal distance both above and *below* the horizontal line; *Bacterium Zopfii* may, in fact, readily extend downwards upon a surface, but it always does so in irregular masses. These results disappointed us at first, until on closer examination we found that in every case parallel threads *passed into the gelatine* almost invariably at the common angle of 45°. These geotropic threads had formed just as quickly as those found on the surface of the gelatine in the case of test-tube cultures; indeed, so rapid is their growth into the gelatine that they may extend a distance of $\frac{3}{4}$ to 1 inch in 12 hours. The symmetrical ingrowing into the gelatine we had also observed in the case of test-tube cultures where the growth upon the surface had been retarded by lowness of temperature, whilst painting the test-tube black in the manner previously referred to appeared to still further increase the inward growth. Fig. 7 is a view of the *back* of an early growth to show the regular ingrowing tendency; but photographs of the more perfect cases are impossible owing to the extreme delicacy of the filaments; fig. 5 is a later stage of 7. In fig. 6 the ingrowing is partially seen, and, as fast as the growth extended upon the surface, fresh rami projected symmetrically into the gelatine. We noticed in some cases that the filaments, after having penetrated the gelatine

and come in contact with the glass surface, might branch and be deflected back parallel to the ingrowing rami.

*Growth upon Agar.*—As stated above, we have never obtained a symmetrical growth in or upon this medium with or without glycerine. The growth is that figured in photograph 10. It takes place slowly, and the margins are irregular, being formed of scattered clumps of the bacterium.

*Growth upon Potato.*—Fig. 9 represents a potato culture; the faintly yellowish-white growth is observed to have no definite geotropic arrangement. The potato, it will be observed, appears black; this has been produced by means of iodine, a method which we have employed with success in demonstrating delicate growths upon potato surfaces.

*Growth in Broth.*—In broth abundant flocculi are formed.

*Growth in Animals.*—We have recorded how this micro-organism was first discovered by Kurth in the alimentary tract of the hen; whilst in our own case it was present in very great abundance in the pus of both the middle ears of the cat. It is just possible that in the latter (present) case the microbe gained access to the ear by the Eustachian tube, and therefore that the bacterium was originally in the mouth. It is conceivable, therefore, that it may, in common with the numerous other *Cladothrix* forms, be of more frequent occurrence in the mouth than is suspected. We have, however, made no observation upon this point. We inoculated two rabbits subcutaneously without result, and in another case the third of a test-tube full of a broth culture was injected into the peritoneum with like lack of success. These few experiments, however, prove little.

*The Action of Oxygen and Carbonic Acid Gas upon* Bacterium Zopfii.—We have already brought forward sufficient facts to show how sensitive this micro-organism is to changes of temperature. Fig. 11 represents a three days old growth in a test-tube kept in an atmosphere of carbonic acid gas; there is simply thickening of the original streak. Control test-tubes which were placed in oxygen at the same time exhibited well marked symmetrical growths from 12 to 24 hours. Further, if the tube in which the growth had been inhibited by the $CO_2$ were transferred to oxygen, a symmetrical growth occurred, as in fig. 12.

*The Action of the Spectrum upon the Growth of* Bacterium Zopfii.*—By means of a Zeiss sub-stage spectroscope a large spectrum was projected through the micro-photographic camera and focussed upon a Petri box of gelatine, across which a streak inoculation was made. From our results so far with gelatine or agar we can only say that

* For assistance in these experiments we are indebted to Dr. Fakirji Surveyor, who, with one of us, is engaged in the study of the action of the spectrum upon the pathogenic organisms.

the growth does not appear to be affected by any of the colours. Some of those who have seen our results think there is more growth towards the blue end; others, on the other hand, towards the red end. We ourselves have come to no definite conclusion as yet.

*Microscopic Characters of the Cultures in the various Nutrient Media.*—The series of photographs which illustrate these points have been fixed and stained in the gelatine, as previously mentioned. We have divided them into three groups. The first group, figs. 15 to 20, represent the *filamentous phase* of the early growth; fig. 17, for example, representing the long segments observed in the rapidly growing pinnate filaments. Groups II and III quickly follow upon the first. Group II, figs. 21 to 23, we venture to call the *skein phase*, which we think corresponds to the *état enchevêtré* of Billet. Group III, figs. 24—31, we think represent the *zoöglea phase*. There yet remains a fourth group, which we have not represented, and in which the segments live an independent existence (as partly shown in fig. 18) and very often are freely motile. We would call this the *dissociated phase*, the *état dissocié* of Billet. We have in this system of group phase division, therefore, followed Billet.* Whether this is a reasonable method of division will have to be judged from our photographs, from certain peculiarities exhibited by the above-mentioned groups, and lastly and chiefly from further examples.

In figs. 15 and 16, Zeiss obj., mm. 75 without eyepiece, the original streak of inoculation and the branches which spring from it are seen. The streak presents interesting peculiarities. Very slight liquefaction of the gelatine may be observed in it, and then very commonly swarming obtains; as previously mentioned, the motile segments may vary very greatly in length. In the figures in question clumps of bacilli occupy the central streak. In some cases, however, long zoöglea-like twisted masses, like those seen in fig. 25, run straight along this streak, it thus appearing as if their direction had been determined by the inoculating needle. In other cases the central streak is a mass of round zoögleaform collections. It will be seen that the micro-photographs in the first group afford very little evidence of the negatively geotropic tendency of the filaments, only the slight amount depicted in fig. 15 being often seen. The thicker branches in figs. 15 and 16, and all the branches in figs. 24 and 25, have assumed the zoögleaform condition. The microscopic picture presented by the rapidly growing pinnate form differs very markedly from these; in it nearly all the fibres in the field run parallel to one another, the microscopic picture then quite coinciding with the microscopic appearance seen, say, in fig. 1 or 14. In the pinnate forms it is exceedingly difficult to trace the origin of the fibres in the central line as well as to follow out the mode of branching; this is

* *Loc. cit.*

chiefly owing to the filaments slightly burrowing into the gelatine. The filaments may be very long and unbranched, but when branching does occur it appears to be brought about as in *Cladothrix* by the deflection of a segment to one side and subsequent growth. Soon after they are formed the long slender rami exhibit a remarkable proneness to twist and to segment, and then to pass into the zoögleaform or, less commonly, into the skein phases. The twisting is very striking, and some idea of it can be gathered from figs. 19, 25, 26, 27, 28, 29, 30. In none of these photos is the spirilliform twist of single filaments shown; it is, however, exceedingly common; the spiral is nevertheless seen in the zoöglea phases, figs. 25, 26, 30. There are, therefore, twists in the horizontal plane, and spirilliform twists. Concerning these twists it appears very remarkable that the majority appear to turn *inwards*, that is, in the opposite direction to the hands of the clock. To this point we will return when discussing the geotropism. It will be gathered from the above and from the photos that the segments may exhibit the "*form phases*" long ago laid stress upon by Zopf and Lankester; we need not, therefore, dwell upon them. The spiral is a striking feature in all gelatine preparations, but is only slightly marked in agar, whilst we have not as yet observed it in broth; but, we may add, we have not examined a sufficient number of these latter specimens.

*Skein Phases.*—The meaning which we wish to convey in this name is set forth in figs. 21, 22, and 23. We lay no stress upon it, but the term is convenient, for it is the form which can, we think, always be seen upon agar and stiff gelatine. It will be seen that it is quite unlike the zoögleaform phase. The filaments composing it are not held together by a common cementing substance, but are formed by plaits taking place in the course of a filament, as seen in figs. 21 and 19. Fig. 23 from an agar culture will at once recall the medusiform appearance of the anthrax growth. Its formation appears to be very closely related to the *stiffness* of the medium upon which it is growing, and appears always to occur *upon the surface of the medium;* the skeins are usually moist, and to the eye present a glistening frosted appearance.

*Zoögleaform Phases.*—This is the phase one commonly sees upon gelatine, and its striking appearance is well represented in figs. 24—31. Zoögleas are said to result from either the aggregation of dissociated elements or from the multiplication of segments which remain where they are formed, being held together by a common cementing substance. Of the former mode of formation we have no experience, and we venture to think that it is not common. If one turns to the descriptions of the higher bacteria, the impression is gained that the zoöglea masses have resulted from local multiplication; that this is so in *Bacterium Zopfii* the photographs show, as

well as the experiment of mixing a small quantity of the bacterium in liquefied sterile gelatine and then pouring it into a Petri dish; in the latter case numerous zoögleaform colonies develop in the solid gelatine, and send out branches which ramify in all directions. The branching zoöglea of *Cladothrix dichotoma*, commonly known as *Zoöglea ramigera*, follows closely the arrangement and branching of the filamentous stage; similarly, the "linear, globose, arborescent, reticular, and tesselated aggregations" of the *Bacterium rubescens* of Lankester probably represent local cell aggregation. As our figures show, the mode of aggregation leads to various forms, but they usually possess one feature in common, and that is spirillation, and a large number may be aptly compared to the twisted strands of a rope. The segments of which they are composed are small bacteroid or coccal forms, and they appear to be formed by the deflection and division of the minute segments into which the original single filaments break up. They rapidly follow the filamentous growth in the symmetrical pinnate cultivations; like the filaments which precede them, they assume the geotropic position. They may extend great lengths and be quite unbranched, or branching may occur as in figs. 30 and 31. Like the filaments, they form in the gelatine; we have not observed them in agar or broth. In fig. 31 a sarcina-like arrangement of the segments is seen; this is of interest, because, as Billet has pointed out, the sarcina of the lower bacteria probably is the representative of the zoöglea phase of the higher bacteria.

### *Upon the Phenomenon of Negative Geotropism exhibited by* Bacterium Zopfii.

If a tube of gelatine is inoculated with a streak culture and kept in a nearly vertical position, a regular pinnate growth will, in the majority of cases, be obtained, identical with fig. 1. If a series of such tubes are placed at intermediate positions between the vertical and horizontal, it will be found that the growths become more and more irregular as the horizontal is reached. These results we have repeatedly obtained since May, 1892. But apparent failures do occur: *e.g.*, if the gelatine is too stiff, an irregular growth results, as in the case of agar, although the tube is kept vertical; microscopic examination of these irregular growths shows the skein phase. Similarly, if the temperature is low the symmetry is greatly interfered with. Experiments in the same manner with Petri boxes give, when sloped, the appearance already noticed in figs. 2 to 7. The pinnate growth is, in these cases, not so striking on the surface as with test-tube cultures, but, as we have previously remarked, the filaments which penetrate the gelatine ran a perfectly parallel course upwards, at an angle of about 45°, *into the substance of the gelatine;* the same

phenomenon may be observed in test-tubes, especially when the growth upon the surface tends to be irregular. If the Petri boxes are kept horizontal, the surface of the gelatine is soon covered with a quite uniform growth, in which, if rami can be distinguished, they take no particular direction. If, instead of these boxes, glass plate cultures are made, and in which, therefore, the coating of gelatine is necessarily thin, a pinnate growth with rami at the angle of about 45° is never obtained. The chance of getting a symmetrical growth upon a large flat surface is therefore much less than in the case of a test-tube. The explanation is difficult. In the test-tube, the surface of the gelatine has a slight curvature, and one often notices that towards the edge of the Petri dishes, where the gelatine is also slightly curved, the growth is more regular. Inequalities on the surface of the gelatine do cause alterations in the direction of the rami, and in some cases a few of the branches on this account appear to take a positive geotropic position. Thus, in addition to temperature and consistence of substratum, there are other circumstances which may favour or retard a symmetrical growth.

When test-tubes containing streak cultures are placed upon the vertical disc of the clinostat, and revolved at rates between one revolution in 2 minutes to 1 in 1 hour, there is in the first place a partial absence of the delicate rami seen in vertically sloped tubes, and when rami are formed they grow in various directions. Fig. 13 shows the irregular growth which first started, and grew over the middle area of the gelatine, and then the formation at the periphery of delicate rami, which in this case are completely *horizontal*. If a Petri dish is substituted for the test-tube, the result depicted in fig. 8 is obtained, a mode of growth which offers a striking comparison to figs. 2—6. Our results with the clinostat have been invariably the same, and, therefore, accord with what Sachs* obtained with the higher plants when the disc of the clinostat revolved slowly. In his case the direction of growth was neither that induced by gravity nor by centrifugal force. Having repeated these experiments very many times, we next tried Knight's experiment upon the action of centrifugal force upon growing plants. In his paper which was communicated to the Royal Society in 1806, he showed that, if young plants were rotated at rates varying between 80 to 250 times in a minute, that the ascending axis of the plant was centripetal, and the radicle centrifugal. Great was our satisfaction when we found likewise that the rami of *Bacterium Zopfii*, which, from the preceding experiments, we considered negatively geotropic, took a marked centripetal course when rotated in the horizontal at the rate of about 240 revolutions per minute. We obtained, in fact, as fig. 14 shows, much more symmetrical and beautiful results than

* Würzburg, Med.-Phys. Gesellschaft, March, 1872.

in the case of gravity. The angle remains about the same, and on microscopic examination the rami are found in nearly all cases strictly parallel and unbranched.

Our experiments thus show that we get a pinnate growth of *Bacterium Zopfii* when the surface of the medium is kept in or near the vertical, or when the culture is rapidly rotated in the horizontal. That an irregular growth obtains when the gelatine surface is horizontal, or when it is slowly rotated in the vertical. That it is necessary in order to demonstrate the upward growth to have a suitable temperature and suitable medium, and that other factors, the nature of which we do not understand, probably likewise influence the symmetrical growth. We would also draw attention to the fact that on vertical or nearly vertical gelatine surfaces, an irregular growth usually spreads *downwards* (compare fig. 6) upon the surface, and that when a horizontal surface of gelatine is inoculated, extension of the organism takes place vertically downwards into the substance of the gelatine; but in neither of these cases are the well-defined rami present. The question now remains, is the force which induces the upward growth of the protoplasmic threads of *Bacterium Zopfii*, *gravity?* Rozanoff* brought forward a beautiful example of upward growth in one of the Myxomycetes, *Æthalium septicum*. He grew it upon a nearly vertical surface of filter paper through which a very slow stream of water must have been constantly passing, as the upper edge of the paper rested in water. He found that the fungus grew upwards. He repeated Knight's centrifugal experiment, and found the fungus centripetal; during this experiment the filter paper was kept moist with water, and therefore the latter must have tended to fly outwards. He grew the *Æthalium* upon a horizontal surface of paper, *across* which a slow stream passed from one side to the other, and he found that growth did not take place more against the stream than with the stream. He argued whether this was an example of negative geotropism or of growth induced by the *contrary stream of water*, and he concluded that *Æthalium* was negatively geotropic, but that the *contrary flow of water* acted like the force of gravity and of centrifugalism. To our minds this does not seem an illogical conclusion, but Strasburger maintained that it was an example of *rheotropism* alone. Rheotropism, as far as fluid is concerned, cannot enter into our case. Our tubes were always plugged with absorbent cotton wool, and were not capped, and we never noticed moisture upon the surface of the gelatine, and, in any case, the geotropic rami tend to very slightly or deeply penetrate the gelatine. We have stated that both in vertical and centrifugalised gelatine growths, rami tend to pass *deeply into* the gelatine. Now we have observed, when we have placed in the

* 'Mém. Soc. Imp. des Sciences, Cherbourg,' vol. 14.

glass dishes gelatine to the depth of 1 inch or more, that at the lower portion of the streak of inoculation the rami which penetrated the gelatine were very distinctly more horizontal than those higher up. This phenomenon is also very conspicuously marked in the case of *centrifugalised tubes*. Further, our great difficulty in connexion with centrifugalising gelatine is to keep it in position, for in a large number of our experiments the gelatine is forced to the bottom of the tube, and the cotton plug is often driven some distance into the tube. We can see, further, that the compression to which the gelatine is subjected increases towards the distal end of the tube. Towards the distal end, however, the rami tend to become more horizontal, so it seems very much as if the tension of the gelatine caused the increased deviation to the horizontal. Having gone so far, we may ask why the rami are not orthogeotropic. We have many times called attention to the fact that the delicate filaments tend always to dip under the gelatine, and it may possibly be that it is the resistance of the gelatine which causes the deviation from the vertical to the curious angle of about 45°. We may here mention that this fact of the tendency to penetrate the gelatine is in apparent contradiction to the fact, that, as our experiments showed, $CO_2$ hinders and O favours symmetrical growth. Now, as a matter of fact, very little growth is obtained from a *stab* culture, so, therefore, it appears necessary that *some portion* of the growth should be close to or freely in contact with the air, and this obtains in *streak* cultures. To return to the action of the resistance of the gelatine, we have called attention to the fact that, next to the pinnate form of growth, the most striking feature in the life of *Bacterium Zopfii* is the tendency to curl. Kurth attributes this fact to the resistance of the gelatine. Now the twisting and the geotropic position of the rami we find tend to go hand in hand; they both tend to disappear upon agar or hard gelatine. Zopf noticed the absence of twisted forms in fluid. We find, as has been above stated, that the majority of the twists are in a direction contrary to the hands of a clock; many of the photographs show this, and these were taken at a time before we had directed our attention to the nature of the twist. Amongst the higher plants the inward twist is the commoner, and various theories have been made to account for the twisting. If we examine the rami which penetrate the gelatine we note that if they tend to be curved they tend to be convex on the lower surface, and that thus we tend to have two surfaces, a dorsal and a ventral, and can imagine with the botanist a difference in the tension of the protoplasm on these sides of the filament. According to De Vries, whose paper from the Wurtzburg Institute we have not been able to obtain, geotropism is not an improbable factor in the production of coils (Sachs). Wortmann* also

* "Theorie des Windens," 'Bot. Zeitung,' 1886

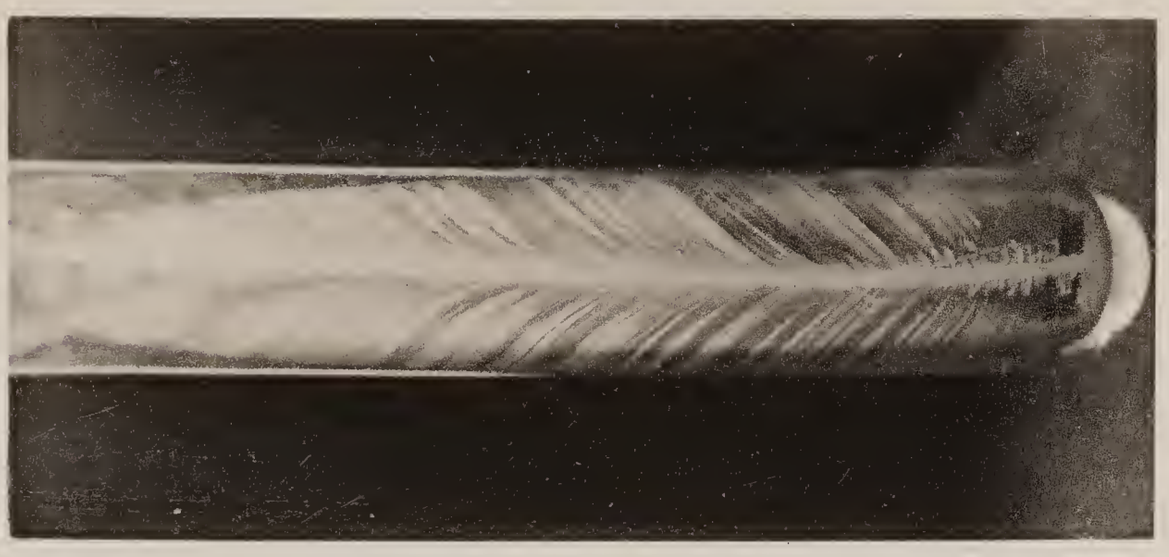

*Fig.* 14.

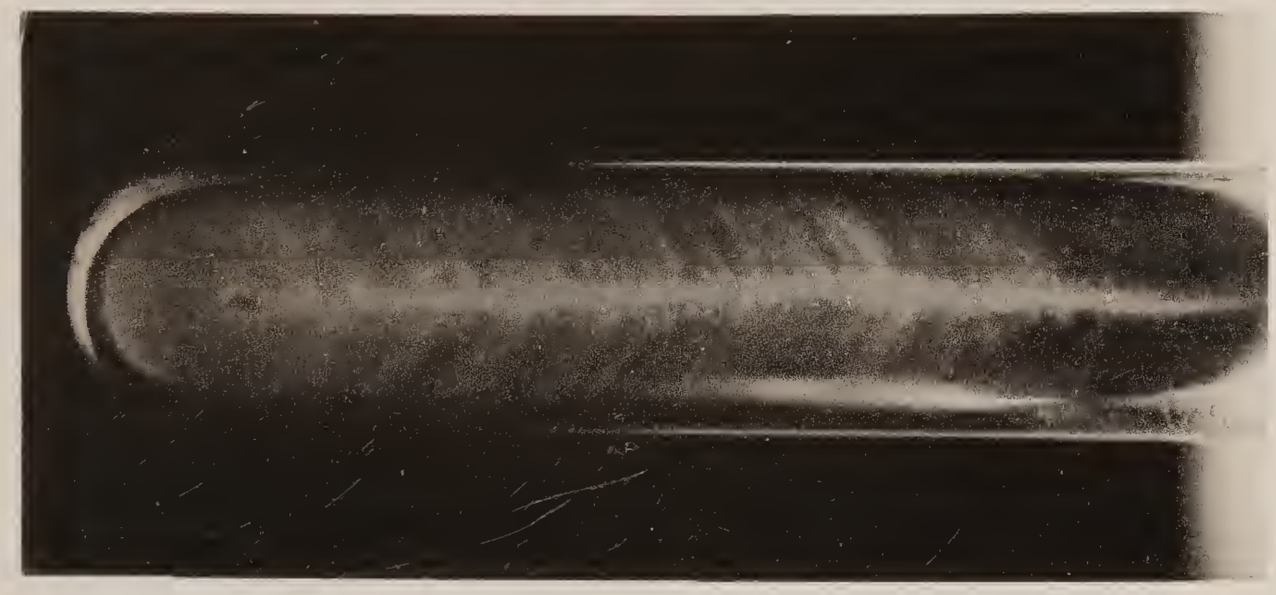

*Fig.* 12.

*Fig.* 10.

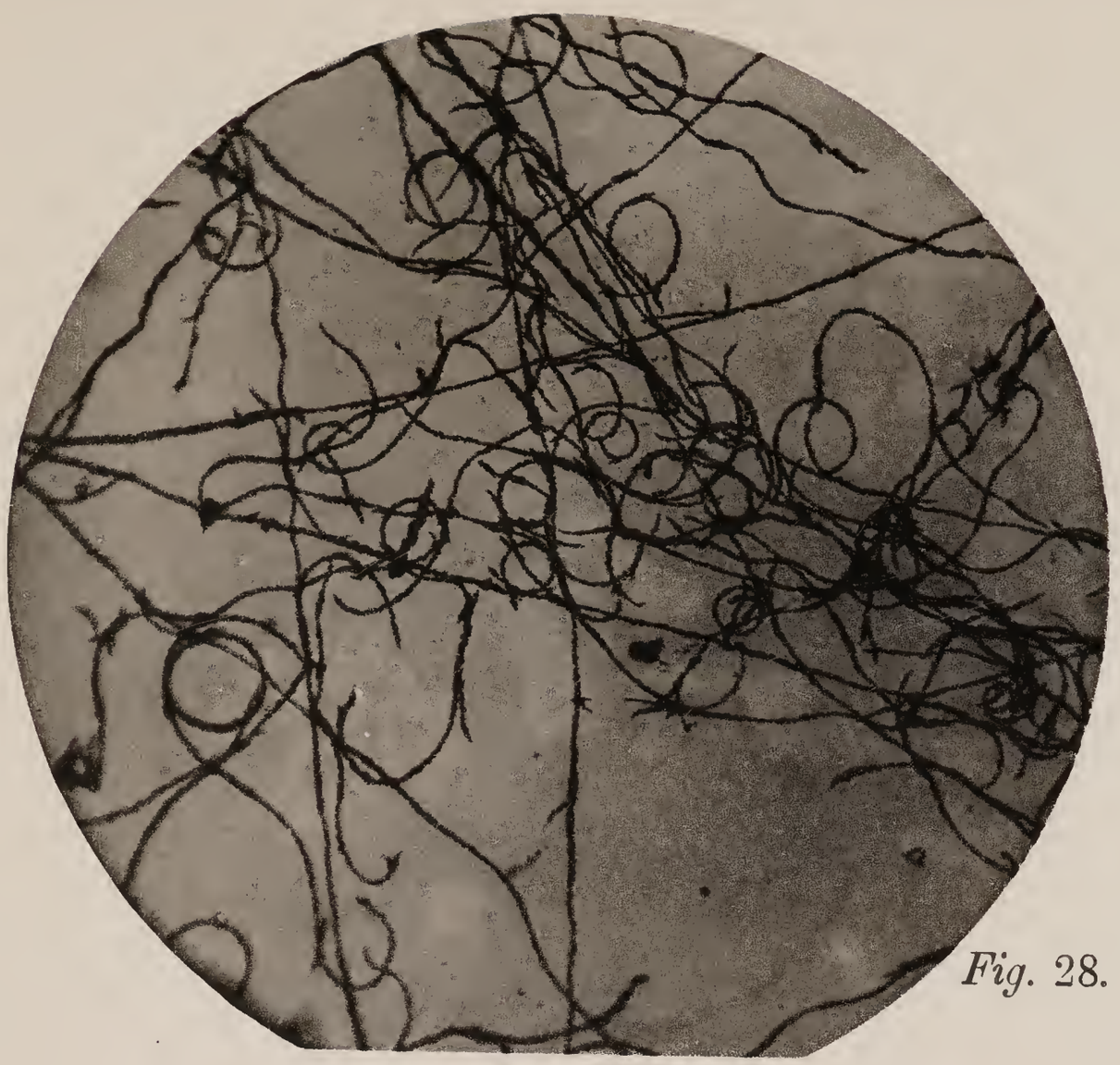

*Fig.* 28.

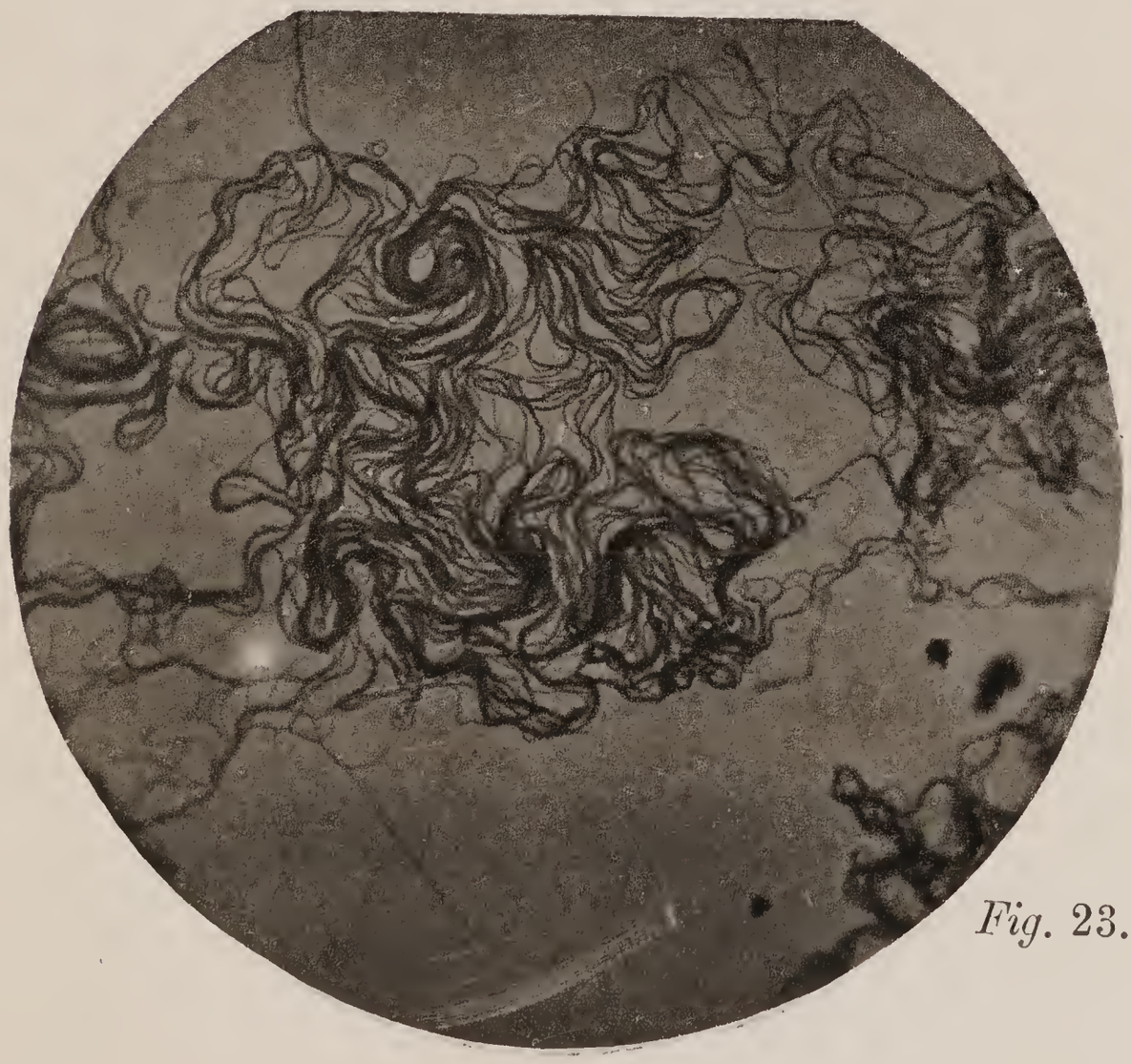

*Fig.* 23.

regards coiling as the result of geotropism, and a second factor which he terms rotating mutation. In our case the coils may be related to the resistance of the gelatine and the negative geotropism. But spirillar forms are well known throughout the microphytes; they are present in *Cladothrix* and many more lowly-organised forms, and are found abundantly in fluid. Do, therefore, the spiral forms which we have described as forming in the gelatine correspond to the free spiral forms of the above examples? If they do, and we have not sufficient evidence to say they correspond, then the forces concerned in their formation in the one case would be equally applicable to the other.

## DESCRIPTION OF PLATES.

PLATE 1. FIG. 10.—Represents a vertical streak inoculation upon agar. The irregular growth is characteristic.

FIG. 12.—This represents a culture which was first grown in an atmosphere of carbonic acid, and the only growth obtained was the thick irregular streak seen along the centre of the tube. It was then transferred to oxygen, and a pinnate growth obtained, as in the figure.

FIG. 14.—A typical symmetrical growth obtained by centrifugalising the culture tube in the horizontal.

PLATE 2. FIG. 23.—Skein, or Medusa-like growth, obtained upon agar.

FIG. 28.—Zooglea threads, showing the phenomenon of twisting. Gelatine growth.

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(Aus dem patholog. Institut des University College in London.)

# Eine neue Streptothrixart, gefunden bei der weissen Varietät des Madurafusses.

Von

Rubert Boyce,

Assistant Professor of Pathology am University College in London.

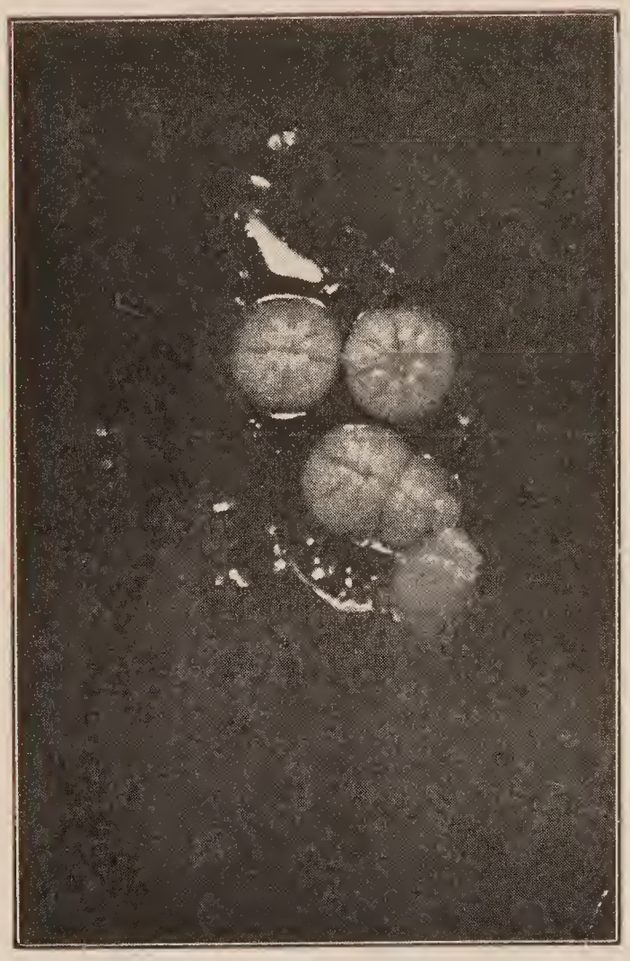
Im Februar v. J.[1]) wiesen Dr. Nusserwanji Surveyor und ich bei der unter dem Namen „Madura foot“ bekannten Krankheit zwei verschiedene Arten von Pilzen nach. Wir constatirten, dass die schwarze Varietät sich in allen Fällen als ein Pilz darstellt, der reich verzweigte Anordnung erkennen lässt, sehr geneigt ist, eine besondere schwarze Pigmentmetamorphose einzugehen und innerhalb des Gewebes, durch Behandlung der Schnitte mit Eau de Javelle, leicht zur Darstellung gebracht werden kann. Andrerseits fanden wir, dass die weisse Varietät aus einem sehr zarten Mycelium besteht, welches in Schnitten sehr dem Actinomycespilz gleicht und hiermit von Einigen sogar identificirt oder wenigstens als zu derselben Gruppe gehörig angesehen wurde (Carter, Kanthack, Hewlett). Wir selbst gaben zwar die Aehnlichkeit zu, betonten aber einige Verschiedenheiten, welche wir damals allerdings noch nicht genügend mit Beweisen belegen konnten.

Seitdem ist es mir nun, durch die gütige Mitwirkung des Lt. Colonel Keith und seines Assistenten, Dr. Boccaro, in Hyderabad, ermöglicht worden, eine Reihe von Züchtungsversuchen auf künstlichen Nährböden vorzunehmen. Zahlreiche Agarröhrchen, welche mit der schwarzen und weissen Art beimpft, uns von Zeit zu Zeit übersandt wurden, zeigten in der grossen Mehrzahl der Fälle eine so starke Verunreinigung durch andere Microorganismen, dass von dem Aussaatmaterial nicht mehr viel zu erkennen war. Nur ein Glas aus einer Serie, welche in Hyderabad mit der weissen Varietät beschickt war, zeigte sich frei von fremden Pilzen. Dagegen hatte das zur Aussaat benutzte Partikelchen durch Entwicklung neuer Colonieen augenscheinlich an Ausdehnung zugenommen. Weitere Culturen wurden sogleich auf Glycerin- und Traubenzucker-Agar angelegt und zugleich eine mikroskopische Untersuchung vorgenommen.

Mikroskopische Untersuchung: Das frische Stückchen besteht aus einem sehr dichten Mycel, welches ziemlich fest ist und sich nur schwer zerzupfen lässt. Innerhalb des Protoplasmas sind Vacuolen erkennbar, die Zellmembran ist sehr dünn, besondere Septa habe ich nicht wahrnehmen können. Keulenbildung ist nicht vorhanden, ebensowenig, soweit ich wenigstens beobachten konnte, eine Bildung coccenartiger oder bacillärer Formen. Die Fäden zeigen eine echte dichotomische Verzweigung, wie das Genus Streptothrix.

[1]) Proceedings of the Royal Society 1893. Transactions of the Royal Society. April 1894.

Züchtungsversuche: Die Züchtung gelingt leicht auf Glycerin- und Traubenzucker-Agar, das Optimum der Temperatur liegt zwischen 35 und 37°. Das Wachsthum erfolgt sehr langsam, viel langsamer als das der Cladothrix asteroides, alba, dichotoma oder Actinomyces. Dasselbe ist besonders characteristisch durch das Auftreten kleiner eigenthümlicher Colonieen, welche langsam auf der Oberfläche des Nährbodens erscheinen. Wie man auf der Photographie leicht erkennen kann, ist bei jeder Colonie eine besondere Lappung zu unterscheiden, zuerst in 4 quadratische Abschnitte, dann in 8 u. s. w., bis später die Colonie aus vielen Lappen besteht und erhaben erscheint. Ein Verschmelzen der einzelnen Colonieen findet nicht statt. Auf Kartoffeln oder in Bouillon (alkalisch oder sauer) bleibt das Wachsthum beinahe gänzlich aus. Auf Kartoffeln und Agar habe ich keine Pigmentbildung beobachtet. Das Wachsthum unterscheidet sich also von den oben erwähnten Cladothrixarten und Actinomyces. Eine Vergleichung der Culturen mit den Partikelchen, welche direct vom Fuss genommen sind, lässt grosse Aehnlichkeit erkennen, da beide aus einer Menge einzelner Lappen bestehen, welche leicht von einander zu trennen sind.



Colonieen des Pilzes, der von der weissen Varietät des „Madura foot“ (Mycetoma) erhalten wurde. 10 Tage altes Obj. 75 mm reflectirtes Licht.

Impfversuche: Subcutane Impfung ruft bei Kaninchen, Meerschweinchen, Affen und Ratten immer locale Reaction hervor, in Gestalt eines Tumors, der in den ersten 2—3 Wochen an Grösse zunimmt, dann aber kleiner und härter wird. Schnitte durch den Tumor zeigen, dass er aus einer Menge von Leukocyten besteht, die das eingeführte Impfmaterial umgeben. Allgemeine Infection habe ich noch nicht beobachtet, was nicht verwunderlich ist, wenn wir die ausserordentlich chronische und rein locale Natur der Krankheit beim Menschen berücksichtigen.

Aus dem Mitgetheilten geht hervor, dass dieser Pilz eine neue Art darstellt, welche als die Ursache der weissen Varietät der Madurakrankheit in Hyderabad anzusehen ist.

Ich sehe mich veranlasst, diese kurze Notiz zu veröffentlichen, weil ich gerade durch die Güte des Herrn Dr. Dünschmann eine Cultur von einem Fadenpilz erhalten habe, welchen Herr Dr. Vincent aus der weissen Varietät gezüchtet hat. Dieser Pilz ist dem meinigen etwas ähnlich (er kann aber Pigment bilden) und mag wohl eine Abart desselben sein. Herr Dr. Vincent hat ihn aus Algier erhalten und inzwischen in den Annalen des Institut Pasteur (1894 No. 3) einen Aufsatz über die weisse Varietät veröffentlicht.

*Reprinted from the 'Transactions of the Pathological Society of London,'* 1893.

# *On cell enclosures in cancer.*

By Rubert Boyce, M.B., and Arthur Giles, M.D., communicated by Dr. Boyce.

[With Plates VI and VII.]

In this short paper it is not our intention to review the work which has been done upon the subject of the numerous bodies found in carcinoma, and the explanation of which has proved difficult. We have, however, in going over the literature, convinced ourselves that a large number of observers have described and figured the same curious bodies, and that it was by no means left to Soudakewitch to discover a specific body. We were fortunate to obtain from Mr. White, of University College Hospital, a carcinoma of the pancreas which presented cell anomalies and cell inclusions in unusual numbers, and we have succeeded in obtaining a large series of microphotographs. In these photographs the bodies described by Soudakewitch, Ruffer, Burchardt, and numerous others may be readily recognised, but they also bring out stages which scarcely fit in with the life history of a parasite; they, moreover, show that the cells which contain these so-called parasites are enormously hypertrophied, both as regards their chromatin and cell plasma, and that consequently we should be as much justified in discussing the "cell inclusions" as additional signs of the activity of these cells, as we should be in regarding the hypertrophy and hyperchromatosis as due to the invasion and subsequent growth of a genuine parasite.

If we go back to the early observations of Malassez we find that strong comparisons are drawn between the tumours in which these bodies are observed in man, and those met with in the familiar coccidium disease of the rabbit. We have looked in vain for strong evidence of this. The coccidium in the liver may be associated, on the one hand, with caseous and necrotic changes, and with a papillomatous and cystic condition of the bile-ducts on the other hand. But how unlike carcinoma are these simple papillomatous changes has been recently emphasised by

Felsenthal and Stamm in 'Virchow's Archiv' for April, 1893. These observers agree that the coccidia may be the indirect causes of the papillomatous growths; that this is very probable the numerous observations upon other animal parasites, such as the distomata, clearly show. The finding of the cancer bodies in the metastases in man shows how very different must be the mode of action of the "parasite" in man. Symbiosis must, therefore, be had recourse to; but when we pass in review the examples of this in the animal kingdom we find the parasite producing little tissue reaction; we have nothing equivalent to the phenomena observed in cancer and sarcoma. There is a great gap between the hyperplasia due to the irritative action of a parasite, and neoplasia due to symbiosis. Few would be found to deny the former, but surely we must look for strong evidence of the latter before we accept such an interesting solution. The "parasite" of cancer has not been cultivated, and the results of inoculation are negative; reliance is therefore placed upon certain staining reactions, upon the undoubted "Eigenthümlichkeit" of the cell enclosures, and upon appearances in these bodies which have been been held to represent phases in the life history of a genuine parasite. We venture to think that it is rash, with such evidence, to so strongly maintain the parasitic nature of these bodies, and to dogmatise upon their intimate relationship to the neoplasm still more reprehensible. At the present stage we should only be concerned with the facts about these bodies, and that is the one reason we have in publishing the photographic record of our simple case. The photographs (Plates VI and VII) show a very curious series of phenomena, which evidence in the future may clearly show to belong to a parasite; in the present paper, however, we wish to demonstrate what can be said in favour of their cell origin.

The processes of cell invagination and of nuclear and cell-plasma degeneration have been discussed by those holding the parasitic view, but endogenous cell-formation must be sharply differentiated from parasitic enclosures, for the endogenous cell and the parasite are alike nucleated protoplasmic masses, and the unicellular parasites of certain mollusca, as well as those found occasionally in the alimentary tract and lungs of man, show how very difficult it is to distinguish the parasites from certain cells of the host. Failure to do so has led, on the one hand, to the mistaking of the parasites of the blood-corpuscles of the frog for active phenomena

of the protoplasm of the corpuscles themselves; and, on the other hand, certain nuclear forms have been regarded as parasites (Bütschli).

Arnold has described and figured endogenous cell-formation in the giant-cells of marrow, of tuberculous glands, and of neoplasms. This phenomenon resembled closely the appearances of parasitism described by recent observers. Müller, working in Arnold's laboratory, has come to the conclusion that the bodies described by Drs. Ruffer and Walker as parasites were typical examples of endogenous cell-formation. Müller's figures and those exhibited by us agree, and their characteristic features may be thus summarised:

1. The cell enclosures are met with in abnormal cells, they are usually giant-cells; there is very often more than one nucleus; there is marked hyperchromatosis, which is characteristic of many forms of sarcoma and carcinoma cells; there are evident signs in many of the giant-cells of dropsy of the plasma. This dropsical condition is represented by a loose reticulum of the cell substance, or by the formation of groups of vacuoles.

2. The cell enclosures are single or multiple, and they usually commence in or near the nucleus, and they may occupy the place of the nucleus.

3. The enclosures consist either of little else than chromatin granules, or of a nucleus and protoplasm. The chromatin of the enclosed bodies may be broken up into several pieces, or appear as if about to divide (Steinhaus, 'Virchow's Archiv,' 1891). The chromatin may be separated by an enclosing vacuole from the rest of the cell, and often stains like the nucleolus of the mother-nucleus.

4. There is a capsule; this is regarded by Dr. Ruffer as formed by the cancer cell itself, and with this we agree. Flemming showed that the capsule of the fat-cell may be highly differentiated and stain characteristically.

5. The capsule expands either by the growth of the enclosed cells, or by the accumulation of fluid. The capsules may, in fact, contain perfect cell enclosures, large or small granular masses, round homogeneous bodies, fine granular *débris*, or only fluid. Compare the changes in the nuclear substance in molluscum contagiosum.

6. When several capsules are formed in the same cell, or in close proximity, a mulberry mass results, comparable to the mulberry

fat-cells (derived from one cell) of certain of the lower animals. The partitions may rupture and fusion may occur.

7. Capsules are met with enclosing more than one nucleated body, or two or more perfectly formed cells; the enclosures themselves may be cystic, and enclose other bodies.

8. There is not the least trace of irritation or leucocytic reaction in the neighbourhood of the cell enclosures.

Finally, cancer bodies have been freely compared with, and called sporozoa, but cancer bodies and sporozoa are in marked contrast in the following points:

1. The intra-cellular sporozoa (sarcosporidia) seem to be of a harmless nature, not causing inconvenience to their host (Bütschli), but rather living on terms of symbiosis.

2. Sarcosporidia are nearly always large, and often visible to the naked eye.

3. The cystic or resting stage of sporozoa is the only one represented at all definitely among cancer bodies; the active amœboid stage, pseudopodial or ciliated forms, as observed in coccidia and klossia, are never seen.

4. The numerous round, lenticular, or falciform spores are not seen in cancer in man.

5. The bodies which are compared to spores are clear, like fat-globules, and of unequal size; the spores of sarcosporidia are invariably of uniform size, and generally granular.

6. The spores of gregarinidæ always have a siliceous, or chitinous, and well-marked capsule. *March 7th*, 1893.

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## DESCRIPTION OF PLATES VI AND VII.

(Reproductions in collotype of photographs taken by Dr. R. Boyce.)

The figures illustrate what the authors regard as varieties of endogenous cell-formation. They are taken from a case of Carcinoma of the Pancreas, and are equally magnified (Zeiss, oc. 1 mm.).

### PLATE VI.

Fig. 1.—Hypertrophied cell. The nucleolus is very large. There are a few scattered chromatin granules in the cell substance close to the nucleus.

Fig. 2.—In this hypertrophied cell the chromatin particle is encapsuled.

Fig. 3.—Hypertrophied cell with two nuclei and large nucleoli. The encapsuled chromatin body is much larger than in the last preparation, and presents the appearance of an enclosed cell. There is evidence of œdema of the cell-substance of the large cell.

Fig. 4.—Hypertrophied cell showing numerous encapsuled bodies of various sizes.

Fig. 5.—In this hypertrophied cell the enclosed body has the characters of a daughter cell.

Fig. 6.—The endogenous daughter cells have grown, and produced atrophy of the mother cell. Observe that one of the endogenous cells is œdematous and vacuolated, and that the other possesses a nucleus and nucleolus.

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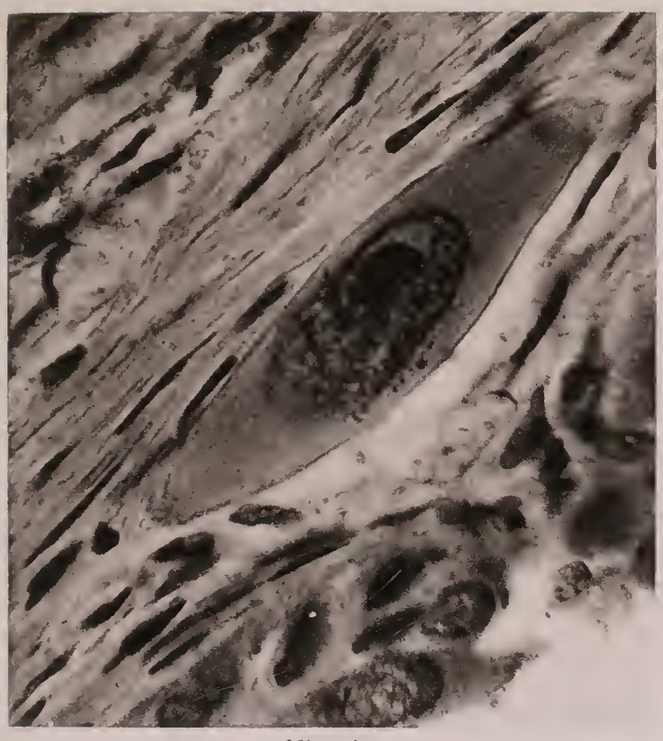

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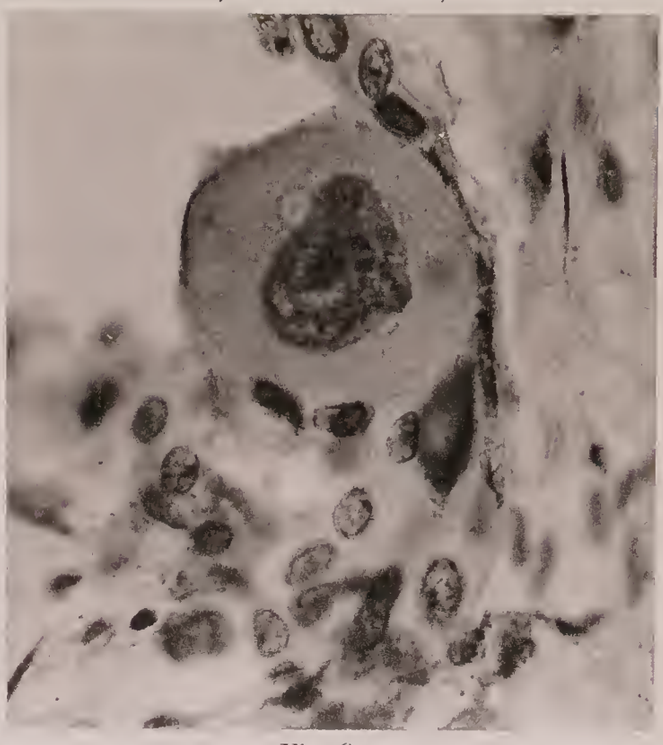

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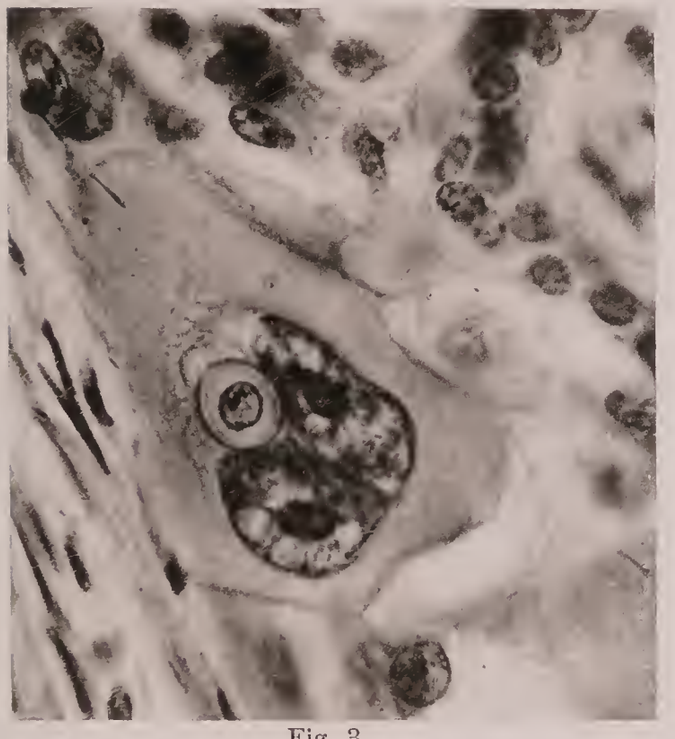

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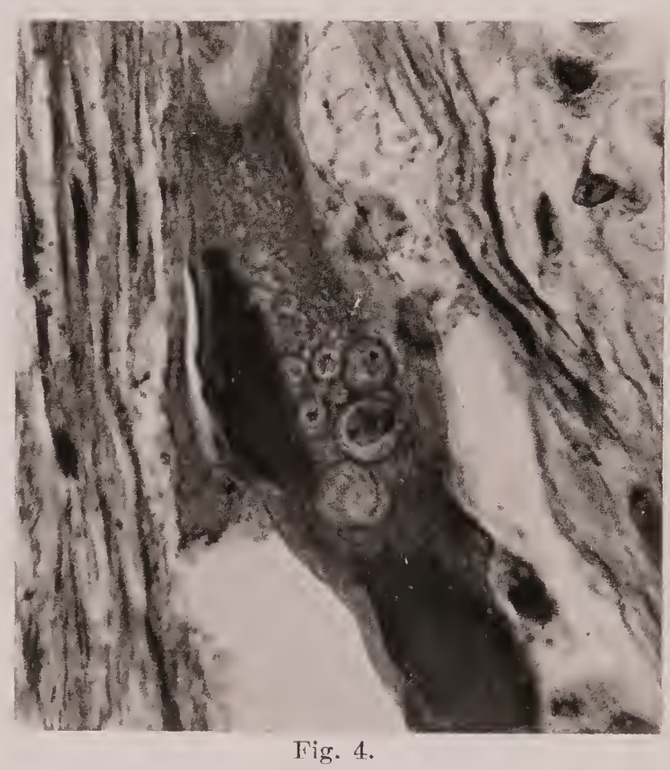


Fig. 4.

Fig. 5.

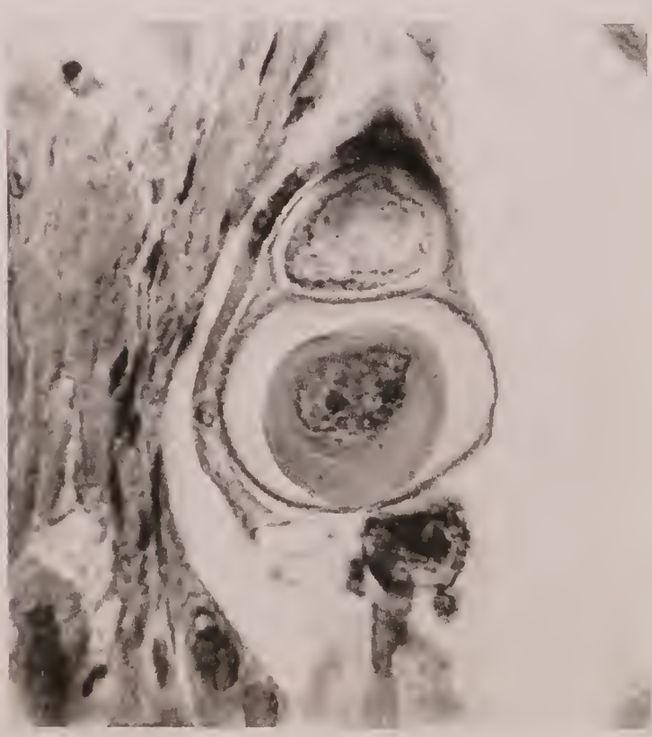


Fig. 6.

## DESCRIPTION OF PLATES VI AND VII.

(Reproductions in collotype of photographs taken by Dr. R. Boyce.)

The figures illustrate what the authors regard as varieties of endogenous cell-formation. They are taken from a case of Carcinoma of the Pancreas, and are equally magnified (Zeiss, oc. 1 mm.).

### PLATE VII.

FIG. 7.—Hypertrophied cell. The nucleus is very large. There are two endogenous cells; one is almost liberated, the other lies in a cystic space, bounded by a deeply staining capsule. This enclosed daughter cell is nucleated and encloses a daughter cell of its own.

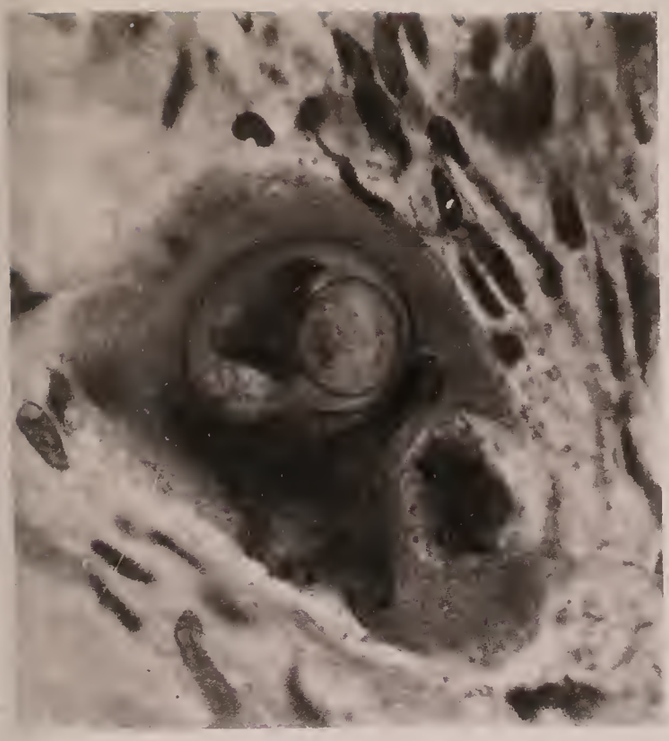
FIG. 8.—Mulberry form of hypertrophied cell, produced probably by the dilatation of the cystic spaces, enclosing chromatin fragments.

FIG. 9.—Cell with three enclosures.

FIG. 10.—Hypertrophied cell with marked vacuolation; some of the vacuoles have contents.

FIG. 11.—Cystic dilatation of cancer cells; the contents are granular, and have a spore-like appearance.

FIG. 12.—In this case the cystic dilatation is much greater; the enclosed cells appear degenerate.



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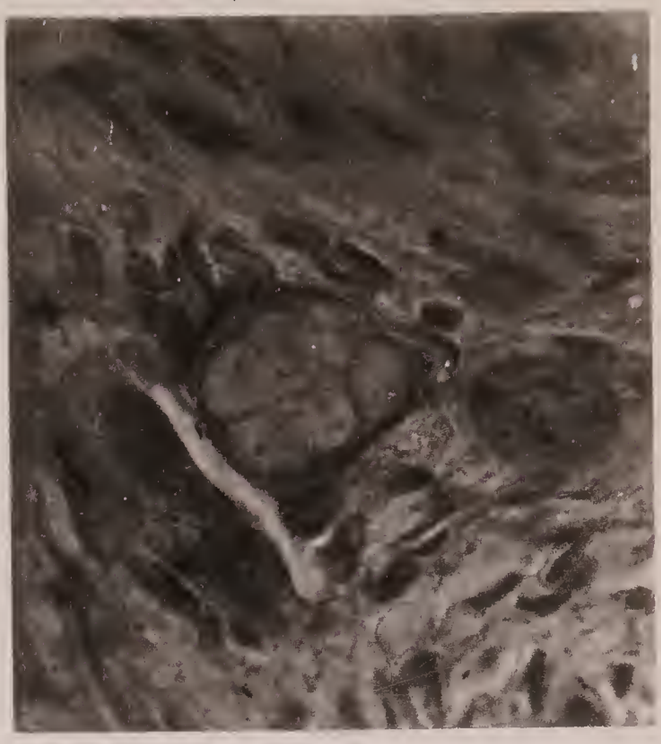

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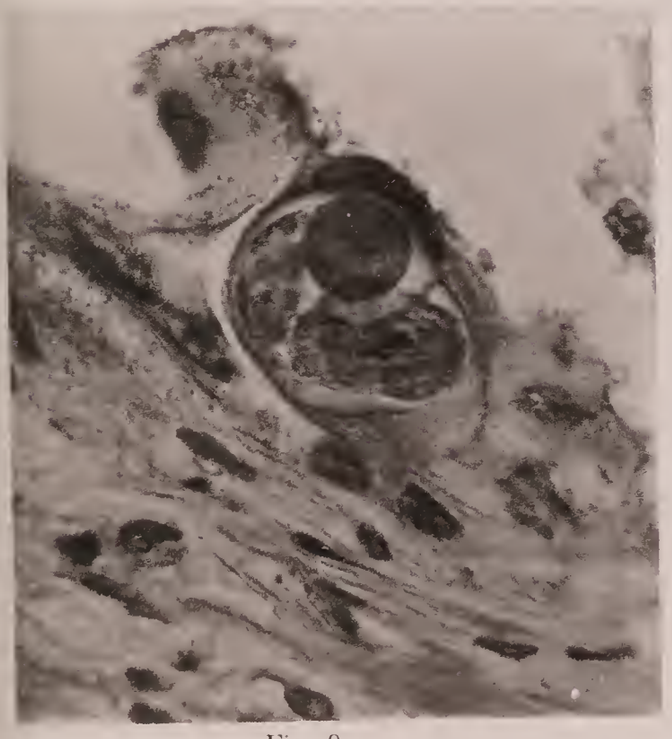

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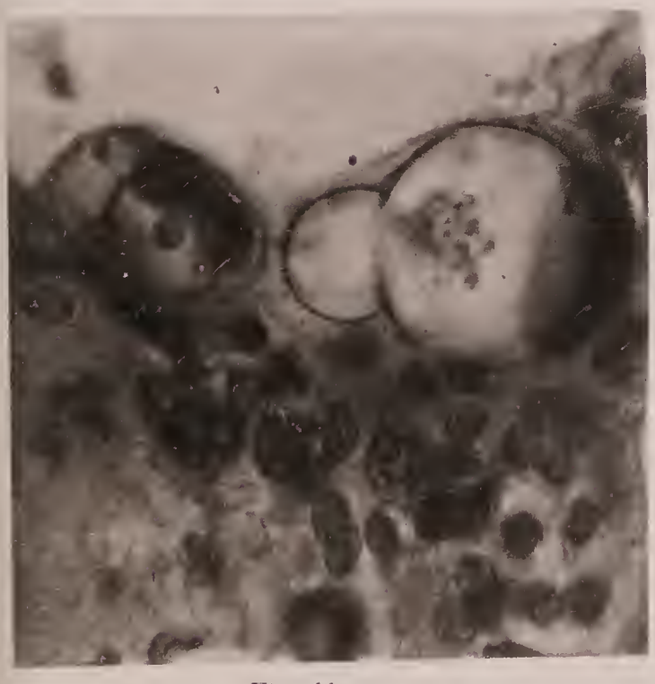

Fig. 11.

Fig. 12.

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